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Assessing Human Health Risks from Chemically Contaminated Fish and Shellfish:

A Guidance Manual

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Introduction

Contamination of aquatic resources by toxic chemicals is a well recognized problem in many parts of the U.S. High concentrations of potentially toxic chemicals have been found in sediments and in aquatic organisms from Puget Sound, the Southern California Bight, northeast Atlantic coastal waters, the Hudson River, the Great Lakes, and elsewhere (Malins et al. 1984; Brown et al. 1985b; DeVault et al. 1986; Capuzzo et al. 1987). Heavy consumption of contaminated fisheries products by humans may pose a substantial health risk. This concern has prompted recent studies of catch and consumption patterns for recreational fisheries and associated health risks (e.g., Puffer et al. 1982; Humphrey 1983, 1987, 1988; Sonzogni and Swain 1984; Swain 1988).

To protect the health of consumers of fish and shellfish, information is needed on relative health risks associated with various edible aquatic species, geographic locations, and consumption rates. In the past, diverse models have been used to estimate human health risks from exposure to toxic substances in food [e.g., Cordle et al. 1978; U.S. Office of Technology Assessment 1979; U.S. Environmental Protection Agency (EPA) 1980b; Food Safety Council 1980, 1982; Connor 1984a; Tollefson and Cordle 1986]. In the present report, a standardized procedure is recommended for assessing human health risks from consumption of chemically contaminated fish and shellfish.

Objectives

The purpose of this manual is to provide guidance for health risk assessment related to chemically contaminated fisheries, based on EPA approaches (e.g., U.S. EPA 1980b, 1986a-e, 1987a). The objectives of the guidance manual are to:

- Describe the steps of a health risk assessment procedure for consumption of contaminated fish and shellfish
- Define the conceptual basis for standard toxicological variables [e.g., Carcinogenic Potency Factors or Reference Doses (RfD) for chemicals] and criteria [e.g., U.S. Food and Drug

Administration (FDA) action levels] related to risk assessment, and information sources for updating these values

- Provide guidance on presentation of risk assessment results
- Summarize assumptions and uncertainties of the recommended procedure for risk assessment.

The guidance provided in this manual is directed primarily at risk assessment related to recreational fisheries. Although assessment of human health risks from commercial fisheries products is not addressed specifically in the examples provided herein, the concepts discussed throughout the manual are relevant to risk analysis for commercial fisheries.

This manual provides guidance only, and does not constitute a regulatory requirement of any kind. The technical content is consistent with approved EPA procedures for risk assessment, as published in the Federal Register (U.S. EPA 1986a-e). The guidance manual is intended to describe what EPA believes to be the most scientifically defensible methods for assessing environmental health risks. These are the methods EPA will use in conducting health risk assessments required in its statutorily mandated programs. The relationship between these procedures and risk assessment approaches used by FDA is described briefly in the background section below.

Organization

Background information on available health risk assessment guidance and use of this manual is provided in the remainder of this introduction. An overview of risk assessment is provided in the following section, including a discussion of the distinction between risk assessment and risk management, and a review of their possible uses. The major steps of the risk assessment process recommended herein are described in subsequent sections. Guidance is provided on mathematical models used to estimate chemical exposure and risk. Sources of information on toxic chemicals and model variables are noted. Finally, suggestions for presentation of risk assessment results are provided and uncertainties are summarized.

Background

Risk analysis encompasses both risk assessment and risk management. Risk assessment is a scientifically based procedure to estimate the probability of adverse health effects from a specific exposure to a toxic agent. Risk assessment differs from risk management, although both are elements of regulatory decision-making (National Research Council 1983). Risk assessment provides the scientific basis for public policy and action. In risk management, risks are interpreted in light of legislative, socioeconomic, technical, and political factors, and appropriate controls are determined. Risk management often involves evaluating risks relative to potential benefits associated with an activity and defining an acceptable risk level (i.e., the maximum risk considered tolerable). For example, a risk manager might weigh the risks associated with chemical contamination of fish and shellfish against the health benefits (e.g., decreased risk of heart disease) associated with consumption of fish and shellfish in place of red meat.

1986 EPA Risk Assessment Guidelines

In September 1986, EPA published final guidelines for assessing health risks related to environmental pollutants. The guidelines are in five parts (U.S. EPA 1986a-e):

- Carcinogen Risk Assessment
- Exposure Assessment
- Mutagenicity Risk Assessment
- Health Assessment of Suspect Developmental Toxicants
- Health Risk Assessment of Chemical Mixtures.

These guidelines pertain to health risk assessment for all environmental exposures [e.g., air exposure; ingestion of water or environmentally contaminated foods; and other direct human contact with contaminated soils, water, sediments, or other materials (Federal Register 51 No. 185, p. 34049)]. The guidelines were developed through a 2-year process that included contributions and review by the larger scientific community; full Agency consideration of public comments in response to proposed guidelines on November 23, 1984; and review and approval by the EPA Science Advisory Board (Federal Register 51 No. 185, p. 33992).

While U.S. EPA's risk assessment guidelines (1986a-e) apply to all exposure routes, they do not contain detailed information on application of the basic principles for each exposure route. This guidance manual provides such step-by-step assistance for assessing health risks from exposure through consumption of chemically contaminated aquatic organisms. The guidance is applicable to freshwater, brackish water, and saltwater fish and shellfish. The risk assessment methods recommended in this manual are consistent with the principles set forth in U.S. EPA (1986a-e).

Regulatory Roles and Coordination of Federal, State, and Local Agencies

As described in a recent policy statement by EPA's Risk Assessment Council and FDA (see **Appendix A**), FDA, EPA, and the states have somewhat differing roles in assessing and managing risks from fish consumption. FDA has the lead responsibility for risk management of foods in interstate commerce or other products of national importance including fish and shellfish. For some chemicals in foods (specifically pesticides), EPA assists FDA in performing the technical evaluations that support risk management decisions. The federal government is not directly responsible for managing risks to individuals who consume unusually large amounts of foods not in interstate commerce or foods harvested from locally contaminated areas (e.g., some recreational fisheries). Environmental agencies and health departments at the state and local levels have responsibility for protecting consumers of local fisheries products. These agencies are responsible for issuing public health advisories and regulations related to local fisheries.

Section 408 of the Federal Food, Drug and Cosmetic Act authorizes EPA to establish tolerances (maximum permissible concentrations) or action levels for pesticides in raw agricultural commodities, including fish and shellfish. FDA is responsible for setting action levels and tolerances for concentrations of other chemicals in fish, shellfish, or other foods. FDA also has responsibility for enforcing the guidelines developed by both EPA and FDA, which may involve removal of adulterated foods (i.e., foods contaminated in excess of an action level or tolerance) from interstate commerce. An action level is the minimum concentration of chemical in food that may be cause for FDA to take enforcement action. An action level is promulgated when a tolerance or exemption authorizing the presence of a substance in food has not been established or has been revoked. Action levels are established and revised according to criteria in the Code of Federal Regulations (21 CFR 109 and 509). An action level is revoked when a formal tolerance for the same substance is established. In developing action levels and tolerances, FDA and EPA take into account both the magnitude of the health risks to consumers and the economic impacts of banning food from a particular source. FDA and EPA set limits on chemical contaminants in fisheries products to achieve an optimal balance of health protection and minimization of economic impacts on food-producing and harvesting industries (e.g., commercial fisheries and fish marketers).

All action levels and tolerances to date have been developed to provide national protection rather than on a regional or local basis. These national standards protect the average consumer of a food product, assuming the consumer eats foods from a typical "national market basket" (U.S. FDA 1984). Action levels and tolerances are not intended to protect certain local subpopulations, such as individuals whose consumption of fish and shellfish from a given water body may exceed the national average (**Appendix A**).

EPA and FDA recognized the need to coordinate their activities and guidance in assessing health risks from contaminated fish and shellfish. The Standing Committee on Fish Contamination has been formed to resolve potential differences in risk assessment calculations for specific chemicals or specific exposure situations (**Appendix A**). The EPA/FDA policy statement in **Appendix A** provides further discussion of the evolving coordination between EPA, FDA, other federal agencies, and the states. The EPA/FDA policy statement also describes procedures whereby states can obtain further information or assistance pertaining to risk management in specific local situations.

Applicability of this Guidance Manual

EPA's nonregulatory technical guidance, including this manual and the 1986 final guidelines for risk assessment (U.S. EPA 1986a-e), is available to state and local governments responsible for fisheries management, environmental protection, and public health. This manual is intended for use as a handbook by those state and local agencies that are responsible for assessing potential risks from local fish or shellfish consumption. For example, it may be useful in assessing risks to highly exposed regional populations (e.g., certain fishermen or families who may eat unusually large amounts of fish). This manual does not provide guidance on policy issues that are beyond the scope of the technical

risk assessment process (e.g., selection of acceptable risk levels, and methods for performing local cost-benefit analyses).

For specific technical assistance in applying the risk assessment methods described in this manual, users may contact EPA national offices (see the last page of **Appendix A**) for updated information on regional EPA facilities that can provide on-site assistance in applying risk assessment techniques.

Relationship of this Manual to Other EPA Documents

This manual is not intended as an exhaustive guide to all aspects of sampling, statistical design, laboratory analysis, exposure assessment, and toxicological risk analysis. Citations are provided to references that provide details on these topics. In addition, several other EPA documents that provide relevant information are listed below:

- U.S. EPA (1987a) *Integrated Risk Information System (IRIS) Manual* - A regularly updated electronic database on the toxicity and carcinogenicity of individual chemicals (see **Appendix B** herein)
- General guidelines on exposure and risk assessment (U.S. EPA 1986a-e).
- Guidance documents on risk assessment approaches for specific chemicals [e.g., dioxins and dibenzofurans (Bellin and Barnes 1986)].
- *Superfund Risk Assessment Information Directory* (U.S. EPA 1986g).
- *Risk Assessment, Management, Communication: A Guide to Selected Sources* (U.S. EPA 1987b) - A general bibliography which is updated periodically.

It should also be noted that the National Oceanic and Atmospheric Administration (NOAA), FDA, and EPA have recently completed a joint study of PCB contamination in Atlantic coast bluefish and potential human health effects (NOAA, FDA, and EPA 1986, 1987). The design of that study, the statistical analysis of the data, and the estimates of dietary intake of PCBs by bluefish anglers and their families provide examples of some of the concepts illustrated in this guidance manual.

Relationship of Fisheries Risk Assessment to Water Quality Standards

Environmental quality guidelines may be developed from risk assessment models to complement available water quality standards. For example, this manual contains recommended procedures for developing guidelines on concentrations of contaminants in edible tissues of fish and shellfish based on risk assessment. Comparisons of data on tissue concentrations of contaminants with such guidelines may be used by state agencies in regulating the harvest, transportation, and sale of fish and shellfish used for human consumption, and in developing health risk advisories. In contrast, state water quality standards are designed to regulate discharges of contaminants to surface waters.

State water quality standards include two primary elements: designated uses and criteria. Recreational fishing and shellfishing are examples of designated uses that may be applied to a water body. Criteria are concentration levels of contaminants in surface water that provide protection from the effects of toxic chemicals, with an ample margin of safety. There are two basic kinds of criteria: those that protect aquatic life and those that protect human health.

The criteria incorporated into state water quality standards are enforceable requirements used by the states to regulate dischargers. In support of the state programs, and to meet the requirements of Section 304(a) of the Clean Water Act, EPA periodically issues national water quality criteria recommendations for use by the states in setting their enforceable standards. In developing national criteria recommendations to protect public health, EPA considers human exposure to chemical contaminants in fish and shellfish as well as drinking water.

The Criteria and Standards Division of EPA's Office of Water Regulations and Standards is responsible for developing national criteria recommendations under Section 304(a) of the Clean Water Act. The current criteria are summarized in *Quality Criteria for Water - 1986* (U.S. EPA 1986h). The technical procedures for deriving human health criteria for water are described in *Water Quality Criteria Documents, Availability* (U.S. EPA 1980b).

The development of water quality criteria to limit human exposure to contaminants in fish and shellfish requires the translation of the contaminant level not to be exceeded in the animal tissues to a level in the water in which the animal resides. This is accomplished through the use of the bioconcentration factors (BCF). A BCF is a measure of the potential of a chemical to accumulate in biological tissues. A BCF value is defined as the ratio of the concentration of a chemical in tissues of a given aquatic species to the concentration in water. Each chemical BCF may be estimated either directly from the results of bioassay testing or from an octanol-water partitioning coefficient for the chemical, if test data are not available.

The calculation of a water quality criterion to protect human health from exposure to contaminants in fish and shellfish is accomplished through the use of the BCF and toxicological and epidemiological data (e.g., data on the amount, or dose, of the contaminant that results in a defined human health risk). The coefficients used in this manual to define the critical dose or the toxic potency for each chemical (see **Dose-Response Assessment**) are the same as those used to develop water quality criteria. IRIS (U.S. EPA 1987a) is the central location for human health-related data and information used by all EPA programs.

Relationship of Fisheries Risk Assessment to Monitoring Under the Clean Water Act

States routinely conduct chemical analyses of fish and shellfish tissue as part of their environmental monitoring programs. The results of fish contamination monitoring are documented in state reports and in the

National Water Quality Inventory Report to Congress (as required by Section 305(b) of the Clean Water Act). The information presented in this guidance manual can be used to support these activities through the identification of guidelines on levels of contaminants in tissues that correspond to a defined risk to human health (e.g., tolerable risk levels).

In addition to these ongoing monitoring activities, the 1987 amendments to the Clean Water Act, in particular the new Section 304(l), require states to develop lists of impaired waters, identify point source discharges of toxic substances and the amounts of pollutants present, and develop individual control strategies (permits) for each point source discharger. The information in this guidance manual may be useful in evaluating data on concentrations of chemical contaminants in fish and shellfish tissue and associated human health risks to identify waters impaired by toxic contamination.

Relationship of EPA Risk Assessment Methods to FDA Risk Assessment Methods

Because of differences in legislative and regulatory responsibilities among EPA, FDA, and state and local governments, these entities have developed differing procedures for risk assessment and risk management. As an EPA guidance manual, this document presumes the use of standard EPA risk assessment procedures. However, certain procedures recommended in this manual can be modified to make the risk assessment compatible with alternative approaches used by FDA and some states. This section explains how conversion factors can be used to make risk assessment procedures recommended herein compatible with certain assumptions used in FDA risk assessments.

A major difference between EPA and FDA risk assessment approaches concerns the methods for extrapolating the toxic potency of chemicals in small experimental animals (e.g., rats and mice) to estimate potential effects in humans. U.S. EPA (1986a) pointed out several species-specific factors that may influence the response to a carcinogen, including life span, body size, genetic variability, concurrent diseases, and the rates and products of metabolism and excretion. To account for at least some of the differences between experimental animals and humans, the estimate of exposure in laboratory animals is multiplied by a scaling factor to obtain an estimate of equivalent dosage in humans. EPA uses the ratio of animal-to-human surface area, whereas FDA uses the corresponding ratio of body weights as a scaling factor. Thus, EPA uses mg of carcinogen per m^2 body surface area per day as a standardized scale for expressing dosages, whereas FDA uses mg carcinogen per kg body weight per day. This difference in interspecies extrapolation factors results in approximately a five- to ten-fold difference in estimates of carcinogenic potency (and risk) derived by the two agencies.

In recognition of the difficulties that differences in interspecies extrapolation procedures between EPA and FDA may pose for state agencies and others who rely on federal guidance on risk assessment, EPA's Risk Assessment Council and FDA reviewed the pros and cons of their respective methods for dosage scaling. They concluded that

the most appropriate method for interspecies dosage extrapolation may vary depending on exposure conditions and chemicals involved. For example, one procedure may be more realistic for lipophilic chemicals, whereas the other would be more appropriate for hydrophilic chemicals. Differences in target organs (i.e., primary site of toxicity) also affect the preferred extrapolation procedure.

Because the EPA extrapolation procedure results in a higher estimate of risk than the FDA procedure (by approximately an order of magnitude), the former is considered more protective. For most EPA assessments, the surface-area based extrapolation is appropriate. The technical basis for EPA's approach relies primarily on a demonstrated relationship between pharmacological effects (e.g., balance of rates of metabolism and excretion) and body surface area (Pinkel 1958; Freireich et al. 1966; Dedrick 1973). If state or local policymakers decide that the body-weight based extrapolation is more appropriate for local risk management needs, then procedures recommended in this manual can be modified by converting EPA's dose-response data using a ratio of human body weight to surface area. This would allow the risk assessor to use carcinogenic potency factors in EPA's computerized database, IRIS (U.S. EPA 1987a). IRIS is a database maintained by EPA to provide regularly updated toxicological data for use in risk assessment. The use of IRIS would greatly increase the ability of a state to perform risk assessments for chemicals of local concern while increasing consistency among jurisdictions sharing responsibility for common waters.

Although the conversion of EPA estimates of toxic potency to estimates based on equivalent dosage scales related to body weight is not technically complex, the modified procedure should preferably be carried out only by experienced toxicologists. The conversion factor will vary depending on whether the dose-response data were derived from rats or from mice. Thus the original data set must be reviewed to determine an appropriate conversion factor. In general, an EPA estimate of carcinogenic potency would be multiplied by a factor equal to the ratio of surface area per unit body weight (m^2/kg) of the laboratory animal to that of humans. For example, if the EPA carcinogenic potency factor is C and the surface area per unit body weight is X for the laboratory animal and Y for humans, the corresponding potency factor based on dosage scaled to body weight is C multiplied by X divided by Y. Because specific data on surface area are often unavailable, body weight to the two-thirds power is typically used as an estimate of surface area. Note that some EPA carcinogenic potency factors are derived from epidemiological studies and therefore do not require conversion.

Other steps in the process to estimate carcinogenic potencies may vary somewhat among regulatory agencies. For example, different agencies may choose different data sets to derive a carcinogenic potency factor for the same chemical. The mathematical expression used to model the dose-response relationship may also differ among agencies. Hogan and Hoel (1982) and Cothern et al. (1986) discuss various models for extrapolating data from high doses used in laboratory experiments to the low doses of concern in carcinogenic risk assessment. At low doses corresponding to risks of 10^{-2} to 10^{-6} or less, different models may produce results that vary by as much as several orders of magnitude.

Nevertheless, the linearized multistage procedure used by EPA (U.S. EPA 1986a; also see below, **Dose-Response Assessment**) yields results that correspond approximately (within a factor of two) to those produced by the linear model used by FDA. The interagency Subcommittee on Fish Residue Issues of the EPA Risk Assessment Council, which included representatives from FDA, concluded that the differences in procedures for modeling dose-response relationships between EPA and FDA were small relative to the uncertainties in other steps of a risk assessment. Therefore, the EPA/FDA policy statement (**Appendix A** herein) does not discuss procedures to reconcile these differences.

A final distinction between EPA's risk assessment procedures and other potential approaches is that EPA does not yet provide a standardized approach for assessing carcinogenic effects on children and fetuses. Information on perinatal carcinogenicity is presently being developed by EPA and others.

Overview of Risk Assessment and Risk Management

The objective of risk assessment is to estimate the probability of adverse health effects from exposure to a toxic agent. The elements of the risk assessment process and their relationship to risk management are shown in Figure 1. U.S. Office of Technology Assessment (1987) provides a review of general policies and technical approaches of federal agencies in assessing risks to human health associated with exposure to chemicals. Background information on food safety evaluation by Federal and state agencies is provided by U.S. Office of Technology Assessment (1979) and Food Safety Council (1980, 1982). Examples of approaches used by FDA to assess human health risks from toxic chemical exposures are described in Cordle et al. (1978) and Flamm and Winbush (1984).

The following sections provide an overview of the steps in risk assessment, the need for a risk assessment approach to evaluate human health risks from chemically contaminated fisheries, and potential applications of the results of fisheries risk assessment. The general format for risk assessment and all definitions of terms used in this report are consistent with those provided by National Research Council (1983) and U.S. EPA (1986a-e, 1987a).

Major Steps in Risk Assessment

A complete risk assessment includes the following steps:

- **Hazard identification:** Qualitative evaluation of the potential for a substance to cause adverse health effects (e.g., birth defects, cancer) in animals or in humans
- **Dose-response assessment:** Quantitative estimation of the relationship between the dose of a substance and the probability of an adverse health effect

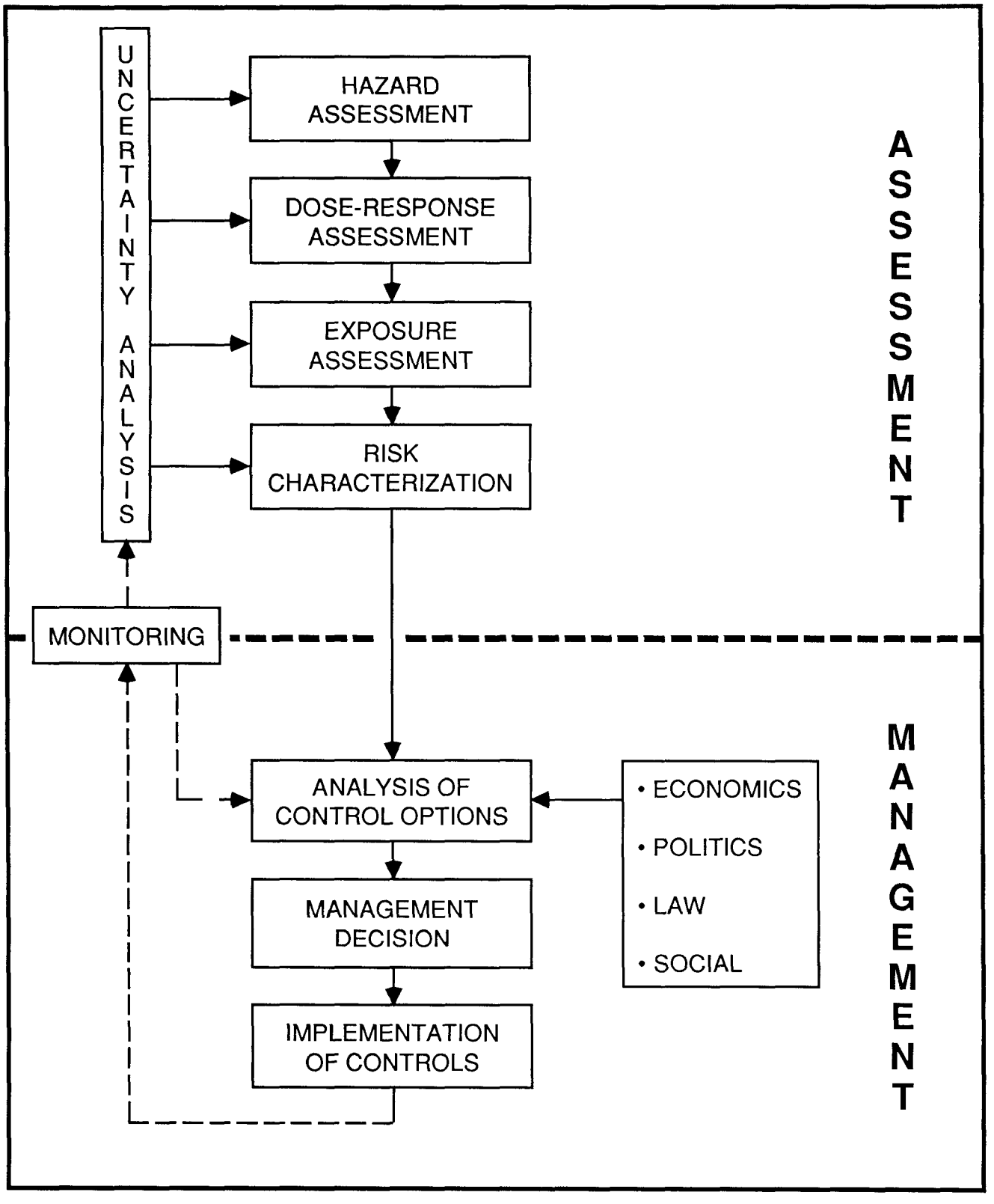


Figure 1. Overview of risk assessment and risk management

- **Exposure assessment:** Characterization of the populations exposed to the toxic chemicals of concern; the environmental transport and fate pathways; and the magnitude, frequency, and duration of exposure
- **Risk characterization:** Integration of qualitative and quantitative information from the first three steps, leading to an estimate of risk for the health effect of concern.

Because uncertainties are pervasive in risk assessment, uncertainty analysis is a key element of each stage of the assessment process. Assumptions and uncertainties are summarized in the risk characterization step. The risk characterization includes a balanced discussion of the strengths and weaknesses of the data presented.

Need for Risk Assessment Approach

Direct measurement of human health risks is possible in certain limited circumstances. Such circumstances generally involve a single high exposure or repeated moderate exposures of humans to a specific chemical with a clear adverse effect. For example, direct measurement of the incidence of chloracne (a skin disorder) might be possible in a population of workers exposed to a PCB spill. In contrast, it is virtually impossible to directly measure the incidence of cancer associated with consumption of chemically contaminated fish or shellfish. The long latency period for cancer, the potential for contamination of fisheries by multiple chemicals, and confounding exposures through other routes would complicate the interpretation of such data. Mathematical models are therefore used by EPA, FDA, the Agency for Toxic Substances and Disease Registry, states, and other regulatory agencies to estimate human health risks from exposure information. Risk assessment procedures discussed in this manual focus on estimating potential health risks from long-term exposure to relatively low levels of contamination. This prospective approach is also useful for developing regulations to limit exposure to toxic chemicals and reduce associated risks.

Scientific knowledge of the effects of toxic chemicals on humans is still rudimentary. Much of the present information is extrapolated from results of laboratory tests on animals (e.g., rats and mice). For example, animal test data may be used to estimate levels of chemical exposure that are unlikely to cause toxic effects in human populations. Toxicologists are faced with many uncertainties when estimating the potential for human health risks associated with intake of toxic chemicals. Despite these uncertainties, regulatory decisions must be made. Many assumptions and subjective judgments may enter into an evaluation of human health risk. The risk assessment approach provides a framework for consistent, systematic estimation of health risks, with clear statements of assumptions and uncertainties.

The risk assessment framework offers an alternative to some common approaches to evaluation of data on chemical residues in fish and shellfish. As noted by Kneip (1983) and Peddicord (1984), many investigators have evaluated chemical residue data in light of human health concerns simply by comparing tissue concentrations of selected

chemicals to action levels or tolerances established by U.S. FDA (1982, 1984). This approach is limited for the following reasons:

- FDA action levels or tolerances are available for only a few chemicals (mercury, 12 organic pesticides or related degradation products, and PCBs).
- FDA has not established regulatory limits for some of the most potent suspected human carcinogens (e.g., 2,3,7,8-tetrachlorodibenzo-*p*-dioxin) or for some of the common contaminants in surface waters (e.g., polynuclear aromatic hydrocarbons and most heavy metals).
- Action levels and tolerances were intended to be used only for regulation of interstate commerce of food products.
- When setting regulatory limits, FDA and EPA consider economic impacts of food regulation as well as the potential human health risks on a national basis (U.S. FDA 1984). When using action levels or tolerances to interpret bioaccumulation data, investigators implicitly adopt economic policies of the federal agencies responsible for setting the limits. Thus, risk management issues at a national level are not clearly separated from site-specific risk assessments.
- Action levels and tolerances were developed from a national perspective. They were not intended to protect localized subpopulations of recreational anglers that may consume contaminated fish or shellfish at a rate substantially above the national per capita average.

Use of regulatory limits on toxic chemicals in food products established by other countries (Nauen 1983) would suffer from many of the limitations listed above for FDA values. Moreover, a concise review of the basis for each of these limits is not available.

Uses of Risk Assessment

Risk assessment may be applied to data on chemical residues in fish and shellfish for the following purposes:

- Identify and rank toxic chemical problems in specific locations
- Develop environmental criteria or guidelines at the national, state, regional, or local level
- Develop public information and advisories.

The first two applications fall within the general category of regulatory decision-making. In this context, one goal of EPA is to define, identify, and set priorities for reducing unacceptable risks. Risk assessment and management provide a framework for balanced analysis of environmental problems (e.g., Tetra Tech 1986a) and consistent policies for reducing health risks (e.g., through reduction of toxic pollutant discharges and cleanup of polluted areas).

Risk assessment can be used to identify and rank environmental problems in several ways. First, contaminated sites can be ranked according to the relative risks associated with consuming fish and

shellfish harvested nearby (e.g., Versar 1985). Site rankings may be used to establish priorities for investigation of contaminant sources and for cleanup. Maps of chemical residue data or risk estimates provide a geographic overview of the condition of resources linked to human exposure. Second, priority chemicals can be identified according to associated health risks or indices of relative hazard (e.g., Ames et al. 1987). Finally, various fishery species and size (or weight) classes within species can be ranked according to relative risks.

Risk assessment is an important analytical tool for developing environmental criteria and guidelines. For example, water quality criteria derived by U.S. EPA (1980b, 1986h) are based in part on human health risk assessment. FDA uses quantitative risk assessment to estimate potential human health risks, which are considered together with economic factors in developing action levels for chemical contaminants in fishery products (U.S. FDA 1984). Risk assessment models can be used to develop guidelines on maximum advisable contaminant concentrations in recreationally harvested species. Such guidelines can contribute to development of target cleanup criteria established to develop remedial actions for contaminated sites.

The results of risk assessments may be used to inform the public about the relative health risks of various fishery species and geographic locations. Providing the recreational public with such information allows for individual choice in determining harvest area, target species, consumption rates, and other factors based on relative risk. Furthermore, risk assessment may contribute to management decisions by federal, state, and local agencies, which may include:

- Investigating sources of pollution
- Reducing exposure potential by implementing pollution controls
- Restricting fishery harvests by geographic area or by species
- Issuing public advisories or controls to limit:
  - Geographic area of harvesting
  - Harvest season
  - Harvest methods
  - Species harvested
  - Catch number
  - Size range harvested
  - Consumption rate.

Further information on the relationship between risk assessment and risk management may be found in Lowrance (1976), U.S. EPA (1984b), Lave and Menkes (1985), Ames et al. (1987), Lave (1987), Russell and Gruber (1987), and Travis et al. (1987).

Hazard Identification

The first step in the risk assessment process is to define toxicological hazards posed by the chemical contaminants in samples of fish and shellfish. These hazards are summarized in a toxicity profile for each contaminant of concern. The EPA chemical database, IRIS, can be easily accessed to obtain summaries of key toxicological data to include in toxicity profiles. The results of the hazard assessment influence the nature and extent of subsequent steps in risk analysis. For example, the endpoint of concern in dose-response assessment may be selected based on the most severe adverse effect identified in the hazard assessment. In the absence of quantitative data for other steps in the risk assessment process, the results of the hazard assessment constitute the final product for a qualitative evaluation of risk.

Contaminants of Concern

The contaminants of concern to be included in a particular risk assessment should be selected based on the following criteria:

- High persistence in the aquatic environment
- High bioaccumulation potential
- High toxicity to humans (or suspected high toxicity to humans based on mammalian bioassays)
- Known sources of contaminant in areas of interest
- High concentrations in previous samples of fish or shellfish from areas of interest.

General information on persistence, bioaccumulation potential, and toxicity may be obtained from references such as Lyman et al.(1982) and Callahan et al. (1979). Other key sources that are periodically updated are the Registry of Toxic Effects of Chemical Substances (e.g., Tatken and Lewis 1983) and the Annual Report on Carcinogens (e.g., National Toxicology Program 1982, 1985). Specific information that is

directly useful in risk assessment can be obtained for many chemicals from IRIS (see below, **Sources of Information** and **Appendix B**).

TABLE 1. Organic Priority Pollutants and 301(h) Pesticides Ranked According to Octanol-Water Partition Coefficients (K_{ow}) (updated from Callahan et al. 1979)

Priority Pollutant	Substance	log(K_{ow})	Reference
69	di-n-octyl phthalate	8.06	m
83	indeno(1,2,3-cd)pyrene	7.66	
89	aldrin	7.40	o
79	benzo(ghi)perylene	7.05	i
111	PCB-1260	6.91	d
--[q]	mirex	6.89	b
75	benzo(k)fluoranene	6.85	
74	benzo(b)fluoranene	6.60	
82	dibezo(a,h)anthracene	6.50	k
107	PCB-1254	6.48	d
73	benzo(a)pyrene	6.42	i
91	chlordane	6.42	i
92	4,4'-DDT	6.36	n
90	dieldrin	6.20	o
129	TCDD (dioxin)	6.10	i
94	4,4'-DDD	6.02	i
106	PCB-1242	6.00	a
72	benzo(a)anthracene	5.91	j
112	PCB-1016	5.88	d
76	chrysene	5.79	j
93	4,4'-DDE	5.69	h
99	endrin aldehyde	5.60	
53	hexachlorocyclopentadiene	5.51	d
9	hexachlorobenzene	5.47	k
100	heptachlor	5.44	d
101	heptachlor expoxide	5.40	d
39	fluoranthene	5.22	j
84	pyrene	5.18	h
41	4-bromophenyl phenyl ether	5.08	g
64	pentachlorophenol	5.00	d
40	4-chlorophenyl phenyl ether	4.92	g
20	2-chloronaphthalene	4.72	g
81	phenanthrene	4.57	h
98	endrin	4.56	d
78	anthracene	4.54	h
109	PCB-1232	4.48	
80	fluorene	4.38	d
--[q]	methoxychlor	4.30	b
52	hexachlorobutadiene	4.28	f
66	bis(2-ethylhexyl)phthalate	4.20	d
68	di-n-butyl phthalate	4.13	m
77	acenaphthylene	4.07	
67	butyl benzyl phthalate	4.05	b
108	PCB-1221	4.00	
8	1,2,4-trichlorobenzene	3.98	k
12	hexachloroethane	3.93	b
1	acenaphthene	3.92	b
102	alpha-HCH	3.85	p

Table 1 (Cont.)

Priority Pollutant	Substance	log(K_{ow})	Reference
103	beta-HCH	3.85	p
104	delta-hexachlorocyclohexane	3.85	h
--[r]	parathion	3.81	e
7	chlorobenzene	3.79	d
105	gamma-HCH	3.72	h
21	2,4,6-trichlorophenol	3.69	c
95	alpha-endosulfan	3.60	
96	beta-endosulfan	3.60	
97	endosulfan sulfate	3.60	
49	fluorotrichloromethane(removed)	3.53	c
26	1,3-dichlorobenzene	3.48	k
25	1,2-dichlorobenzene	3.38	k
27	1,4-dichlorobenzene	3.38	k
55	naphthalene	3.36	h
113	toxaphene	3.30	
38	ethylbenzene	3.15	
62	N-nitrosodiphenylamine	3.13	b
22	para-chloro-meta cresol	3.10	a
31	2,4-dichlorophenol	3.08	a
28	3,3'-dichlorobenzidine	3.02	
37	1,2-diphenylhydrazine	2.94	g
58	4-nitrophenol	2.91	d
--[r]	malathion	2.89	e
60	4,6-dinitro-*o*-cresol	2.85	
6	tetrachloromethane	2.64	d
42	bis(2-chloroisopropyl)ether	2.58	g
85	tetrachloroethene	2.53	b
11	1,1,1-trichloroethane	2.47	b
34	2,4-dimethylphenol	2.42	b
87	trichloroethene	2.42	b
15	1,1,2,2-tetrachloroethane	2.39	b
47	bromoform	2.30	
32	1,2-dichloropropane	2.28	
86	toluene	2.21	b
--[r]	guthion	2.18	
14	1,1,2-trichloroethane	2.18	
24	2-chlorophenol	2.16	b
50	dichlorodifluoromethane (removed)	2.16	c
4	benzene	2.11	d
51	chlorodibromomethane	2.08	
35	2,4-dinitrotoluene	2.00	
36	2,6-dinitrotoluene	2.00	
33	1,3-dichloropropene	1.98	
30	1,2-*trans*-dichloroethene	1.97	c
--[r]	demeton	1.93	
23	chloroform	1.90	b
48	dichlorobromomethane	1.88	
56	nitrobenzene	1.83	b
5	benzidine	1.81	g
13	1,1-dichloroethane	1.78	
57	2-nitrophenol	1.77	
54	isophorone	1.67	b
71	dimethyl phthalate	1.61	b

Table 1 (Cont.)

Priority Pollutant	Substance	log(K_{ow})	Reference
16	chloroethane	1.54	
59	2,4-dinitrophenol	1.53	
29	1,1-dichloroethene	1.48	
65	phenol	1.46	a
10	1,2-dichloroethane	1.45	b
70	diethyl phthalate	1.40	b
63	N-nitrosodipropylamine	1.31	
44	dichloromethane	1.30	
19	2-chloroethylvinylether	1.28	g
43	bis(2-chloroethoxy)methane	1.26	g
3	acrylonitrile	1.20	b
18	bis(2-chloroethyl)ether	1.12	b
46	bromomethane	1.00	
2	acrolein	0.90	b
45	chloromethane	0.90	
88	vinyl chloride	0.60	
61	N-nitrosodimethylamine	-0.58	g

a Veith et al. (1979a).
b Veith et al. (1980).
c Gossett et al. (1983).
d Veith et al. (1979b).
e Kenaga and Goring (1980).
f Leo, A., 20 November 1984, personal communication.
g U.S. EPA (1980b).
h Karickhoff (1981).
i Rapaport and Eisenreich (1984).
j Miller et al. (1985).
k Means et al. (1980).
l Miller et al. (1984).
m McDuffie (1981).
n Chiou et al. (1981).
o Briggs (1981).
p Solubilities of the various isomers of HCH indicate that they will have similar log(K_{ow}) values.
q Chlorinated pesticides that are not on the priority pollutant list but are included in Section 301(h) (Clean Water Act) monitoring programs.
r Organophosphorus pesticides that are not on the priority pollutant list but are included in Section 301(h) (Clean Water Act) monitoring programs.

Recommendations regarding specific contaminants of concern are beyond the scope of this guidance manual. A general list of contaminants with available EPA toxicological data listed in IRIS is provided in **Appendix B**. The procedures for quantitative risk assessment outlined in this manual are designed for use only with chemicals having toxicological indices [Reference Doses (RfD) or Carcinogenic Potency Factors]. In addition to the availability of toxicological indices, the relative bioaccumulation potential of various chemicals is a key consideration in selecting contaminants of concern. EPA priority-pollutant organic chemicals and selected pesticides are listed in Table 1 in descending order of bioaccumulation potential, according to their octanol-water partition coefficients (Tetra Tech 1985a). Note that

organic compounds with a log octanol-water partition coefficient greater than or equal to 2.3 were recommended by Tetra Tech (1985a) for inclusion in EPA Section 301(h) (Clean Water Act) monitoring programs. EPA priority-pollutant metals are listed in Table 2 in descending order of bioaccumulation potential, according to their BCF (Tetra Tech 1985a).

TABLE 2. Inorganic Priority Pollutants Ranked According to Bioconcentration Factor (BCF)

Priority Pollutant No.	Substance	log BCF[a]
123	methylmercury	4.602
123	phenylmercury	4.602
123	mercuric acetate	3.447
120	copper	3.073
128	zinc	2.762
115	arsenic	2.544
118	cadmium	2.513
122	lead	2.253
119	chromium VI	2.190
119	chromium III	2.104
123	mercury	2.000
124	nickel	1.699
127	thallium	1.176
114	antimony	ND
117	beryllium	ND
121	cyanide	ND
125	selenium	ND
126	silver	ND

[a]BCF = Bioconcentraction Factor. The value shown is the geometric mean BCF among studies summarized by Tetra Tech (1985a). U.S. EPA (1986h) provides additional information on BCF values for selected chemicals.
ND = No data.

Screening of potential contaminants of concern should be done on a case-by-case basis during preparation of risk assessments. When data on concentrations of contaminants in edible tissues of fishery organisms are available, preliminary calculations of potential risks may be made to rank chemicals by relative priority for detailed evaluation. If contaminant concentration data are available for soils, air, and water (at a hazardous waste site, for example), U.S. EPA (1986f) methods for selecting indicator chemicals for public health evaluations at Superfund sites may be used to gain perspective on contaminants of concern. For potential carcinogens, the qualitative weight of evidence for carcinogenicity should be considered. Those chemicals with sufficient evidence of carcinogenicity in humans should generally be considered as contaminants of concern.

Toxicity Profiles

Toxicity profiles are summaries of the following information for the selected chemicals of concern:

- Physical-chemical properties (e.g., vapor pressure, octanol-water partition coefficients)

- Metabolic and pharmacokinetic properties (e.g., metabolic degradation products, depuration kinetics)
- Toxicological effects (e.g., target organs, cytotoxicity, carcinogenicity, mutagenicity) according to specific uptake route of concern (i.e., ingestion).

A toxicity profile may consist of an IRIS chemical file. An example file taken from IRIS is provided in **Appendix B.**

The key elements of a hazard assessment should be summarized in a concise tabular format. The examples shown in Table 3 and in the first two sections of the IRIS file (Chronic Systemic Toxicity; Risk Estimates for Carcinogens) in **Appendix B** illustrate the kinds of information used to evaluate toxicological hazards. Neither toxicity profile in Table 3 is intended to be comprehensive.

TABLE 3. Toxicity Profile for Mercury and PCBs[a]

Property	Mercury[b]	PCBs[c]
CAS Number	7439-97-6	1336-36-3
Physical-Chemical		
Molecular weight	200.6 - 318.7	154.2 - 498.7
Vapor pressure (mm Hg)	0.012 - 0.028	2.8 x 10-9 - 7.6 x 10-5
Solubility (mg/L)	0.056 - 400,000	-5.9
Log K_{owd}	N/A[e]	4.0 - 6.9
Log Bioconcentration Factor[d]	2.0 - 4.6	1.9 - 5.2
Carcinogenic Status	Noncarcinogen	Probable human carcinogen[f] Group B2 - Sufficient animal evidence - Inadequate human evidence
Acute Toxicity		
Human LD50 (mg/kg body wt)	29[g]	--
Mammal LD50 (mg/kg body wt)	1.0 - 40.9	1,010 - 16,000
Chronic Toxicological Effects		
Humans	Motor and sensory impairment leading to paralysis, loss of vision and hearing, and death. Kidney dysfunction.	Skin lesions, liver dysfunctions, and sensory neuropathy. Possible reproductive and developmental impairment.
Mammals	Reproductive impairment and teratogenic effects.	Hepatoxicity, fetotoxicity, skin lesions, and hepatocellular carcinoma. Reproductive and developmental impairment.
Critical endpoint for risk assessment	Central nervous system effects (e.g., ataxia and parathesia)[h].	Hepatocellular carcinoma[f].

Table 3 (Cont.)

[a] This is an example toxicity profile and is not intended to be comprehensive.

[b] Mercury may occur in its elemental form, as inorganic salts, or as organic complexes. Consequently, the chemical and toxicological properties vary tremendously depending on the degree of complexation or metal speciation.

[c] Physical-chemical properties and toxicity vary according to the degree of chlorine substitution, the number of adjacent unsubstituted carbons and steric configuration.

[d] Bioconcentration Factors are the ratio of a chemical concentration in tissues of marine or estuarine organisms and the concentration in water to which the organism is exposed (Tetra Tech 1985a).

[e] N/A = not applicable.

[f] U.S. EPA (1980a,b, 1986f; IARC 1978).

[g] For mercury (II) choride via oral route of exposure (Tatken and Lewis 1983). Relevance to consumption of mercury (primarily methylated) in fish is questionable.

[h] Clarkson et al. (1973).

Information in a toxicity profile is used to support the weight of evidence classification for the likelihood of a chemical causing a given health effect. The endpoints considered should include noncarcinogenic as well as carcinogenic effects. EPA has developed a weight-of-evidence classification scheme which indicates the state of knowledge on the carcinogenicity of chemicals (U.S. EPA 1986a, 1987a). It includes the following categories:

- **Group A - Human Carcinogen:** This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agent and cancer.
- **Group B - Probable Human Carcinogen:** This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited." It also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient" evidence of carcinogenicity in animals as presenting a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate" evidence or "no data" from epidemiologic studies would usually be categorized under Group B2.
- **Group C - Possible Human Carcinogen:** This group is used for agents with limited evidence of carcinogenicity in animals in the absence of data on humans. It includes a wide variety of evidence: e.g., (a) a malignant tumor response in a single, well-conducted experiment that does not meet conditions for sufficient evidence; (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting; (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity; and (d) response of marginal statistical significance in a tissue known to have a high or variable background rate.

- **Group D - Not Classifiable as to Human Carcinogenicity:** This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.
- **Group E - Evidence of Noncarcinogenicity for Humans:** This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies. The classification of an agent in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent is not a carcinogen under any circumstances.

The above descriptions for the categories were taken from U.S. EPA (1986a). At present, a weight-of-evidence classification for carcinogenicity is available in IRIS for each chemical assigned a Carcinogenic Potency Factor.

Sources of Information

In many cases, EPA regions and others may rely on toxicity profiles generated previously. IRIS is a key source of chemical toxicity data, including information from critical studies and weight-of-evidence classifications for carcinogens. The first step in a hazard assessment should be to consult IRIS chemical files for potential contaminants of concern. IRIS chemical files are available for approximately 260 chemicals (as of August 1988). Further information on IRIS is provided in **Appendix B.**

The primary sources of toxicity profiles are the EPA Office of Waste Programs Enforcement and Office of Health and Environmental Assessment (e.g., **Appendix C**, Table C-1). EPA toxicity profiles are available for approximately 195 chemicals. Additional sources are shown in **Appendix C**, Table C-2. Under the Superfund Amendments and Reauthorization Act of 1986, EPA and the Agency for Toxic Substances and Disease Registry are preparing toxicity profiles for 100 hazardous substances considered as high priority contaminants at Superfund sites.

Supplementary information on the toxicity of contaminants of concern may be obtained from bibliographic or chemical/toxicological databases. DIALOG, a comprehensive bibliographic database system (Dialog Information Services, Inc., 3460 Hillview Avenue, Palo Alto, CA 94304), offers access to databases such as Pollution Abstracts, National Technical Information Service, and ENVIROLINE. Chemical and toxicological information can be obtained from the databases listed in **Appendix C**, Table C-3. In particular, MEDLARS and its associated databases (e.g., Toxline, RTECS, and AQUIRE) provide extensive toxicological information.

Dose-Response Assessment

After the potential hazard associated with each contaminant of concern is characterized, the relationship between dose of a substance and its biological effect is determined. Dose-response data are used to determine the toxicological potency of a substance, a quantitative measure of its potential to cause a specified biological effect. The concepts of exposure, dose, dose-response relationship, and toxicological potency are discussed in the following sections.

Exposure and Dose

The concepts of exposure and dose, as defined below, are central to risk assessment:

- **Exposure**: Contact by an organism with a chemical or physical agent
- **Dose**: The amount of chemical uptake by an organism over a specified time as a consequence of exposure.

The "ingested dose," or amount of chemical ingested, is distinct from the "absorbed dose." For the oral route of exposure, the absorbed dose is the amount of chemical assimilated by absorption across the lining of the gastrointestinal system. Exposure level or exposure concentration is used to denote the concentration (mg/kg wet weight) of contaminant in edible tissue of fish or shellfish. As shown below, the absorbed dose is estimated from food consumption rate, the exposure concentration, and an absorption coefficient (see **Exposure Assessment**).

Dose-Response Relationships

The form of the dose-response relationship for carcinogens is assumed to be fundamentally different from that for noncarcinogens (U.S. Office of Science and Technology Policy 1985). Examples of general dose-response relationships are shown in Figure 2. The lack of a demonstrated threshold in dose-response relationships for car-

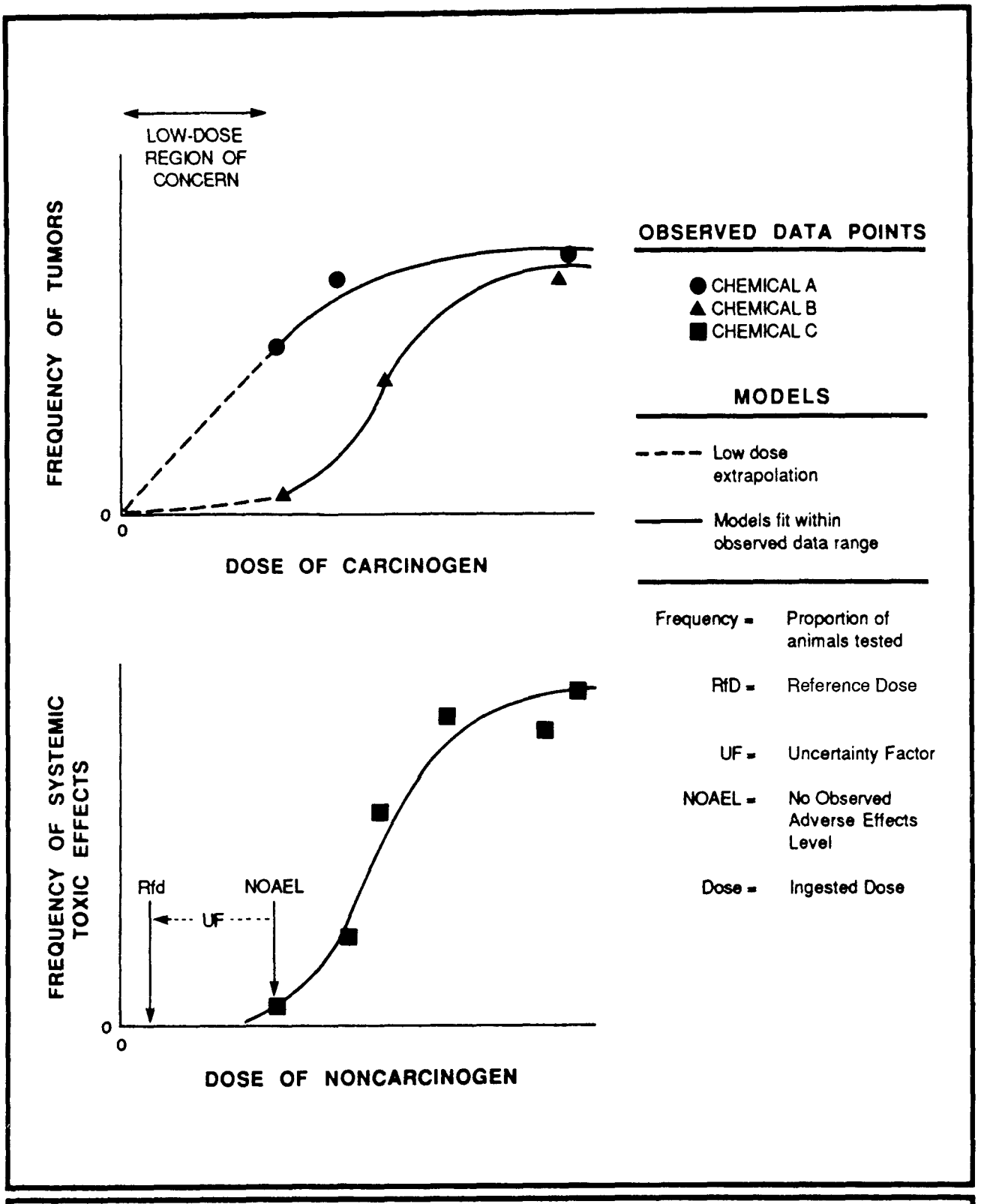


Figure 2 Hypothetical example of dose-response curves for a carcinogen and a noncarcinogen.

cinogens (U.S. EPA 1980b, 1986a; U.S. Office of Science and Technology Policy 1985) implies a finite risk of cancer even at very low doses of the carcinogen. For noncarcinogenic effects, there is usually a threshold dose (i.e., a dose below which no adverse biological effects are observed in the animal bioassay). The threshold dose is termed the No-Observed-Adverse-Effect-Level (NOAEL), as shown in Figure 2. Note that a nonzero mean response may be a NOAEL if that mean response is not significantly different from zero as determined by a statistical test. The Lowest-Observed-Adverse-Effect-Level (LOAEL) is the lowest concentration that results in a statistically significant health effect in the test population.

A measure of toxicological potency is derived from an empirical dose-response relationship for the chemical of interest. Toxicological potency indices for two broad categories of toxicants are defined as follows:

- Carcinogens are individually characterized by a **Carcinogenic Potency Factor**, a measure of the cancer-causing potential of a substance estimated as the upper 95 percent confidence limit of the slope of a straight line calculated by the linearized multistage procedure or another appropriate model
- Noncarcinogens are individually characterized by an RfD, an estimate of the daily exposure to the human population (including sensitive subpopulations) that is unlikely to produce an appreciable risk of adverse health effects during a lifetime.

Carcinogenic Potency Factors are also referred to as Slope Factors. The RfD is conceptually similar to an Acceptable Daily Intake (U.S. EPA 1987a).

The data set used to define toxicological indices is determined by the quality of available data, its relevance to modes of human exposure, the similarity of the species to humans, and other technical factors. Adequate data from clinical or epidemiological studies of humans are preferred over animal data. If adequate human data are not available, a data set for the animal species most similar to humans or for the most sensitive species is used in the dose-response assessment. Data are evaluated by EPA to ensure high quality (e.g., U.S. EPA 1980b, 1985a).

The main source of dose-response data for deriving Carcinogenic Potency Factors and RfDs is lifetime cancer bioassays performed on rats or mice. Because most of these experiments are designed to be cost-effective, doses in bioassays may be orders of magnitude above those encountered in the human environment. High doses are used in laboratory bioassays for several reasons: 1) to reduce the time required to produce a response and thus overcome problems related to latency period (i.e., length of time between exposure and appearance of health effects), 2) to obtain sufficient statistical power to detect health effects, and 3) to decrease the absolute number of animals required and thereby reduce costs. Doses in animal bioassays for oral uptake of contaminants are usually the administered (ingested) dose, not the absorbed dose (i.e., uptake across the lining of the gastrointestinal system).

Carcinogenic Potency Factors and RfD values derived by EPA are listed in the IRIS database. At present, values for these toxicological indices are being standardized for agency-wide use. A brief overview of methods by which these indices are derived is presented below.

Carcinogenic Potency Factors

The Carcinogen Assessment Group of EPA currently uses the linearized multistage procedure to derive Carcinogenic Potency Factors (U.S. EPA 1980b, 1985a, 1986a, 1987a). The multistage model assumes that carcinogenesis results from a series of interactions between the carcinogenic chemical and DNA, with the rate of interactions linearly related to dose. For example, a chemical may induce a mutation in the DNA of a cell to initiate carcinogenesis. However, a series of further interactions between DNA and the same chemical (or another one) may be necessary to promote carcinogenesis and induce a tumor. The multistage model is the model most frequently used by EPA when there is no convincing biological evidence to support application of an alternative model. Other models include the logit, probit, single-hit, and Weibull models (Food Safety Council 1980, 1982; Hogan and Hoel 1982; Cothern et al. 1986). At high doses (corresponding to lifetime risks greater than about 10^{-2}), all currently used models yield generally similar risk estimates. Below risks on the order of 10^{-2}, the models diverge increasingly as dose declines. In the low-dose range, the linearized multistage model generally predicts risks similar to the single-hit (i.e., linear) model. For many data sets, both of these models yield higher estimates of low-dose risk than do other models (U.S. EPA 1980b; Hogan and Hoel 1982; U.S. Office of Science and Technology Policy 1985).

The mathematical form of the multistage model for a specified carcinogen is:

$$R(d) = 1 - \exp[-(q_1 d + q_2 d^2 + \ldots + q_k d^k)] \qquad (1)$$

where:

R(d)	=	Excess lifetime risk of cancer (over background at dose d) (dimensionless)
q_i values	=	Coefficients [kg day mg^{-1} (i.e., the inverse of dose units)]
d	=	Dose (mg kg^{-1} day^{-1})
k	=	Degree of the polynomial used in the multistage model.

U.S. EPA (1987a) described the linearized multistage procedure as follows:

- The multistage model is fitted to the data on tumor incidence vs. dose
- The maximum linear term consistent with the dose-response data is calculated, which essentially defines the linear portion of the dose-response function at low doses

- The coefficient of the maximum linear term, designated as q_1^*, is set equal to the slope of the dose-response function at low doses
- The resulting estimate of q_1^* is used as an upper-bound estimate of the Carcinogenic Potency Factor (termed Slope Factor in U.S. EPA 1987a).

q_1^* is usually calculated as the upper 95 percent confidence limit of the estimate of the coefficient q_1 in Equation 1.

The model commonly used to estimate plausible-upper-limit risk for low levels of exposure over a lifetime is therefore:

$$R^*(d) = q_1^* d \quad (2)$$

where:

$R^*(d)$ = Upper-bound estimate of excess lifetime risk of cancer (dimensionless)

q_1^* = Upper-bound estimate of carcinogenic potency (kg day mg^{-1})

d = Dose (mg kg^{-1} day^{-1}).

Equation 2 represents a linear approximation of the multistage model. Because the slope of the dose-response function at high doses could be different from that at low doses, the use of q_1^* as an upper-bound estimate of potency is not valid at high levels of exposure. Thus, q_1^* should not be used as the upper-bound estimate of potency at exposures corresponding to excess lifetime risks greater than approximately 10^{-2} per individual (i.e., one excess tumor per 100 exposed individuals).

If a potency factor is derived from nonhuman data, as is usually the case, it must be extrapolated to humans. Before being applied to humans, Carcinogenic Potency Factors derived from animal data are corrected using surface-area differences between bioassay animals and humans (U.S. EPA 1980b, 1986a). The rationale for using surface-area extrapolations is detailed in Pinkel (1958), Freireich et al. (1966), Dedrick (1973), and Mantel and Schneiderman (1975). The relationship between surface-area extrapolation and body-weight extrapolation approaches is discussed in the Introduction above (see **Background, Relationship of EPA Risk Assessment Methods to FDA Risk Assessment Methods**).

Reference Doses

Current methods for predicting human health effects from exposure to noncarcinogenic chemicals rely primarily on the concept of an RfD (U.S. EPA 1987a). The RfD is derived from an observed threshold dose (e.g., NOAEL or LOAEL if the NOAEL is indeterminate) in a chronic animal bioassay by applying an uncertainty factor, which usually ranges from 1 to 1,000 (Dourson and Stara 1983). The relationship between the NOAEL, the RfD, and the uncertainty factor are illustrated in Figure 2 above. The uncertainty factor accounts for differences in threshold doses among species, among intraspecies groups differing in sensitivity, and among toxicity experiments of different

duration. Dourson and Stara (1983) and U.S. EPA (1987a) discuss the methods for deriving RfD values and the criteria for selecting uncertainty factors. In brief, an uncertainty factor of 1000 is based on combining a factor of 10 to account for animal-to-human extrapolation, a factor of 10 to protect sensitive individuals, and a factor of 10 to account for use of a LOAEL in place of a NOAEL.

Sources of Information

In many cases, EPA regions and other agencies will be able to rely on dose-response assessments generated previously. Current values for Carcinogenic Potency Factors and RfDs are given in IRIS (U.S. EPA 1987a; e.g., see **Appendix B**). Before using these values, investigators should consult the IRIS database and current EPA health assessment documents for information on their derivation and associated uncertainties. Contacts for information on specific chemicals are listed in IRIS Chemical Files.

Carcinogenic Potency Factors

The Carcinogenic Potency Factors calculated by the EPA Carcinogen Assessment Group are published in IRIS and in each health assessment document produced by the Office of Health and Environmental Assessment (e.g., U.S. EPA 1985a). The EPA Carcinogen Assessment Group develops these carcinogenic potency values and updates them periodically. Before being entered into IRIS, Carcinogenic Potency Factors and supporting documentation are reviewed by the Carcinogen Risk Assessment Verification Endeavor (CRAVE) work group. The list of Carcinogenic Potency Factors published in each health assessment document is intended only to provide comparative information for various chemicals. IRIS should be used as the primary source of Carcinogenic Potency Factors for risk assessment.

Reference Doses

IRIS is the primary source of RfD values. An example of an IRIS data sheet for the pesticide lindane is shown in **Appendix B**. The data sheet provides information on the RfD, the endpoints (biological effects) of concern, experimental data sets, doses, uncertainty factors, additional modifying factors, confidence in the RfD, reference documentation, and dates of agency RfD reviews.

Individual program offices within EPA may need to be consulted for information on chemicals not yet incorporated into IRIS. For example, the Office of Drinking Water is a source of RfDs for selected chemicals. In May 1987, the Office of Drinking Water released draft Health Advisories containing RfDs and guidelines for short-term effects for 16 pesticides: alachlor, chlordane, 1,2-dibromo-3-chloropropane (DBCP), 2,4-dichlorophenoxyacetic acid (2,4-D), 1,2-dichloropropane, endrin, ethylene dibromide (EDB), heptachlor and heptachlor epoxide, lindane, methoxychlor, oxymyl, pentachlorophenol, toxaphene, and 2,4,5-trichlorophenoxypropionic acid (2,4,5-TP). Office of Drinking Water Health Advisories will eventually be incorporated into IRIS.

Exposure Assessment

Exposure assessment is the process of characterizing the human populations exposed to the chemicals of concern, the environmental transport and fate pathways of those chemicals, and the frequency, magnitude, and duration of the exposure dose (U.S. EPA 1986b). For exposure assessment of contaminated fish and shellfish, the following factors should be considered:

- Concentrations of contaminants in aquatic biota of concern
- Potential environmental transfer of contaminants from sources through aquatic species to humans
- Fisheries harvest activities, diet, and other characteristics of exposed human populations
- Numerical variables (e.g., food consumption rate, contaminant absorption efficiency) used in models to estimate exposure
- Purpose of the exposure assessment (e.g., assessment of potential closure of sport or commercial fishery; documentation of health risk from local contaminant sources such as hazardous waste site or wastewater discharges; development of sportfish consumption advisories).

Information on contaminant concentrations and the exposed population is combined to construct an exposure profile, which includes estimates of average rates of contaminant intake by exposed individuals. Key stages of an exposure assessment for contaminated fish and shellfish are discussed in the following sections.

Measurement of Contaminant Concentrations in Tissues

Guidance on development of study designs to measure concentrations of toxic substances in edible tissues of fish and shellfish is provided in

this section. The guidance provided below focuses primarily on field surveys or monitoring programs involving the collection of samples directly from aquatic environments, or from harvesters when the specific geographic origin of samples is known. Such guidance is directly relevant to analysis of recreational fisheries. The present document does not specifically address approaches to marketplace sampling of commercial fisheries products, although some of the concepts discussed below apply to marketplace surveys. Sampling designs for collection of fisheries products from the marketplace are available in FDA Compliance Program Guidance Manuals (e.g., U.S. FDA 1986). Sampling of commercial fisheries directly at the source is preferred over marketplace sampling because the former generally allows documentation of the sampling location.

If the exposure assessment is designed to include contaminant intake from consumption of commercial fish and shellfish, samples may be obtained in two ways. First, samples of target species can be obtained directly from commercial fishermen. In this case, a strict quality assurance/quality control (QA/QC) program should be implemented to ensure proper handling, storage, and documentation of samples. Documentation should include sampling location, species name, size (length, carapace width, or shell height/width), weight, sex, reproductive condition, time and date of sampling, and preservation technique. In most cases, a technician or observer should be on board the fishing vessel to maintain proper sample handling and documentation. Alternatively, samples may be collected by monitoring program personnel using vessels other than commercial fishing boats. In this case, samples should be collected in a way that simulates commercial fishing practices as closely as possible (e.g., same species, size classes, season, fishing area, sampling method, and water depth). Regardless of the general approach to sampling, the organisms collected should be placed directly in temporary storage on board the sampling vessel. Upon return to shore, resection of samples should be accomplished as quickly as possible using an adequate clean-room. If an extended sampling cruise necessitates resectioning on board, an adequate clean-space should be set aside to ensure that samples are not contaminated.

Analysis of chemical residues in tissue to support an exposure assessment is one kind of bioaccumulation study. Bioaccumulation is defined here as the uptake and retention of a contaminant (e.g., a potentially toxic substance) by an organism. The term bioconcentration refers to any case of bioaccumulation wherein the concentration of contaminant in tissue exceeds its concentration in the surrounding medium (i.e., water or sediment). The phrase "bioaccumulation survey" will be used below to refer to measurement of chemical residues in tissue samples from fish and shellfish collected in the field.

The elements of a study design for analysis of chemical residues in tissue include:

- Objectives
- Target species and size (age) class
- Sampling station locations
- Target contaminants

- Sampling times
- Kind of sample (e.g., composite vs. grab, cooked vs. raw; fillet vs. whole organism)
- Sample replication strategy
- Analytical protocols, including detection limits
- Statistical treatment of data.

Because the complexity and specific features of a sampling design will depend on the objectives of the exposure assessment, no single design can be recommended here. Nevertheless, some basic steps in the study design process can be summarized as follows:

- Define concise objectives of the study and any hypotheses to be tested.
- Define spatial and temporal characteristics of fisheries relative to harvesting activities (e.g., seasonality, catch or consumption rates, species composition, size ranges, demersal vs. pelagic species).
- Define harvesting activities and methods of preparing food for consumption that potentially affect exposure to contaminants.
- Define kinds of samples to be collected (species, type of tissue, mode of preparation) and variables to be measured, based on a preliminary exposure analysis.
- Evaluate alternative statistical models for testing hypotheses about spatial and temporal changes in measured variables. Select an appropriate model.
- When possible, use stratified random sampling for each fish and shellfish species, where the different strata represent different habitat types or kinds of harvest areas that may influence the degree of tissue contamination.
- When practical, specify equal numbers of randomly allocated samples for each stratum/treatment combination (e.g., habitat type in combination with species or season).
- Include samples from a relatively uncontaminated reference or control area to help define local contamination problems.
- Perform preliminary sampling or analyze available data to evaluate the adequacy of alternative sampling strategies (e.g., composite samples vs. tissue from individual organisms) and statistical power as a function of the number of replicate samples.
- Develop a QA/QC program that covers: sample collection and handling; chain of custody; data quality specifications; analytical methods and detection limits; data coding; data QA/QC steps to assess precision, accuracy, and completeness; database management specifications; data reporting requirements; and performance audits.
- Define data analysis steps, including statistical tests, data plots, summary tables, and uncertainty analysis.

Note that the second and third steps above depend on information developed as part of the characterization of the exposed population (see **Exposed Population Analysis** below). Also, practical limitations of field sampling may dictate compromises in the sampling design. For example, use of equal sample sizes is generally recommended because statistical analysis of data sets with unequal sample sizes may be difficult or unnecessarily complex. However, collection of equal numbers of replicate samples for each treatment (or stratum) may be impractical if both dominant and rare species are to be sampled at a series of harvest locations with a broad range of harvest yields. Depending on the specific objectives and corresponding study design, a series of statistical analyses rather than a single test may be appropriate.

Detailed guidance on sampling strategies is provided by Phillips (1980), Green (1979), Tetra Tech (1985b,c; 1986b), Phillips and Segar (1986), and Gilbert (1987). Much of the guidance provided in the following sections incorporates the suggestions of these authors.

The statement of objectives is a critical step in the study design process, since specification of other design elements depends on the survey objectives. The study objectives must in turn relate to the objectives of the exposure assessment in which the data will be used. The relationships between study objectives and general features of a sampling design are addressed in the next section.

Study Objectives and General Sampling Design

Specific objectives of a chemical residue study should be defined to ensure collection of appropriate data for the exposure assessment. Different objectives may require radically different sampling designs. Although the primary objective of a field study may be to estimate the mean concentrations of specified chemical contaminants in edible tissues of harvested species, it may be necessary to specify additional objectives to meet the needs of exposure assessment or risk management. For instance, statistical discrimination among mean contaminant concentrations in samples from different harvest areas, seasons, or species may be desired. Such information might be needed to manage relative risks among harvest areas and to impose fisheries closures on a site-specific basis.

Example Objectives--Some examples of objectives for exposure assessments paired with appropriate bioaccumulation survey objectives are given below. These objectives are provided to illustrate the ways in which the elements of a bioaccumulation study design depend on the exposure assessment objectives. They are not intended to be recommended objectives for an actual exposure assessment. In these examples, the bioaccumulation study design involves specifically the measurement of chemical residues in edible tissues of fishery species. Information on the exposed population, including an analysis of their dietary habits (e.g., fisheries species consumed, food preparation method, and consumption rate), is discussed later (see **Exposed Population Analysis**). Such information may influence the objectives of the exposure assessment and the bioaccumulation survey.

Example 1:

- **Exposure Assessment:** Estimate the worst-case exposure for a wide range of contaminants over a predefined geographical area.
- **Bioaccumulation Design:** Estimate mean concentrations of contaminants in edible tissues of a selected narrow size range of individuals of the most contaminated species during the season of peak contaminant concentrations.

Example 1 represents a screening survey to evaluate the need for further work. Edible portions of a limited number (e.g., 3-5) of individual organisms or composite samples would be analyzed for a large number of compounds and the risk assessment conducted assuming moderate or high (but plausible) consumption rates. The species and size range selected would be the ones most likely to accumulate high concentrations of contaminants. Typically, the target species for a screening survey would be the largest individuals of a bottom dwelling species associated with soft sediments.

Example 2:

- **Exposure Assessment:** Estimate the long-term average exposure to each of the contaminants A, B, and C through consumption of aquatic species L, M, N, and O combined from harvest area Z for the average person in the exposed human population.
- **Bioaccumulation Design:** Estimate the mean concentrations of contaminants A, B, and C in edible tissues of aquatic species L, M, N, and O combined from harvest area Z over an annual period.

Example 2 illustrates a simple case involving the consumption of multiple species from a single harvest location. Individual or composite samples of each species would be analyzed separately during different seasons or during a single season expected to represent the annual average. If samples are analyzed separately during different seasons (e.g., see discussion of Example 4 below), the mean annual exposure for all species could still be calculated from the seasonal data. In general, highly composited samples are not recommended because information on different factors (e.g., species, seasons) that affect contaminant concentrations is lost.

Example 3:

- **Exposure Assessment:** Estimate a plausible-upper-limit of exposure to each of the contaminants A, B, and C through consumption of aquatic species L, M, N, and O combined from harvest area Z for a seasonal harvester in the exposed population.
- **Bioaccumulation Design:** Estimate the upper bound of the 95 percent confidence interval of the mean concentration for each of the contaminants A, B, and C in edible tissues of aquatic

species L, M, N, and O combined from harvest area Z during the season of highest contamination.

The general sampling design for the objectives of Example 3 would require replicate composite samples to estimate upper bounds of 95 percent confidence intervals for the mean concentrations of contaminants across species. To meet these objectives, samples could be composited across species, although this is generally not recommended. Multispecies composites would not provide data for assessing exposures corresponding to different dietary habits. To obtain an upper-limit estimate of exposure, it might be sufficient to analyze samples from only one season if available information on seasonal variation was sufficient to select one season as the expected worst case.

Example 4:

- **Exposure Assessment:** Estimate the probability distribution of exposure to each of the contaminants A, B, and C through consumption of each of aquatic species L, M, N, and O from harvest area Z for various segments of an exposed population (e.g., ethnic groups) over an annual period.
- **Bioaccumulation Design:** Estimate the probability distribution of concentrations of contaminants A, B, and C in edible tissues of each of aquatic species L, M, N, and O from harvest area Z over an annual period.

To accomplish the objectives of Example 4, extensive seasonal data on the dietary composition of several subgroups of the exposed population must be available. Separate replicate composite samples of each harvested species could be analyzed for each season. During each season, the species analyzed would correspond to those represented to a significant extent in the diet. Probability (frequency) distributions and means of contaminant concentrations would be derived for each species during each season. By combining data from different species, the probability distribution of exposure and the mean exposure weighted by species representation in the diet could be calculated for each population segment. Note that data to support the analyses required by Example 4 are seldom available before a specially designed study is conducted.

Example 5:

- **Exposure Assessment:** Estimate an average and a plausible-upper-limit of exposure to each of the contaminants A, B, and C through consumption of each of aquatic species L, M, N, and O from each of the harvest areas X, Y, and Z over an annual period.
- **Bioaccumulation Design:** Estimate the mean concentration and the upper bound of the 95 percent confidence interval of the mean concentration for each of the contaminants A, B, and C in edible tissues of each of species L, M, N, and O from each of the harvest areas X, Y, and Z during each of the harvest seasons.

The sampling strategy appropriate for Example 5 is complicated by the occurrence of discrete harvest areas. Replicate composite samples of a given species would generally be required for each season and area in which the species is harvested. Because the characteristics of the exposed population may differ among harvest areas, it may be appropriate to divide the exposed population into segments corresponding to geographic areas, ethnic groups, age classes or other factors. The seasonal and total annual exposure for each segment of the exposed population would be calculated for each species as in Example 4 above.

Influence of Environmental and Population Factors--The four examples just given illustrate the variety of general study designs that may be needed to meet diverse objectives. The specific design of a chemical residue study will depend on the interplay between dietary patterns of the exposed population and environmental factors that influence concentrations of contaminants in tissues of aquatic organisms. Some of the important environmental factors are:

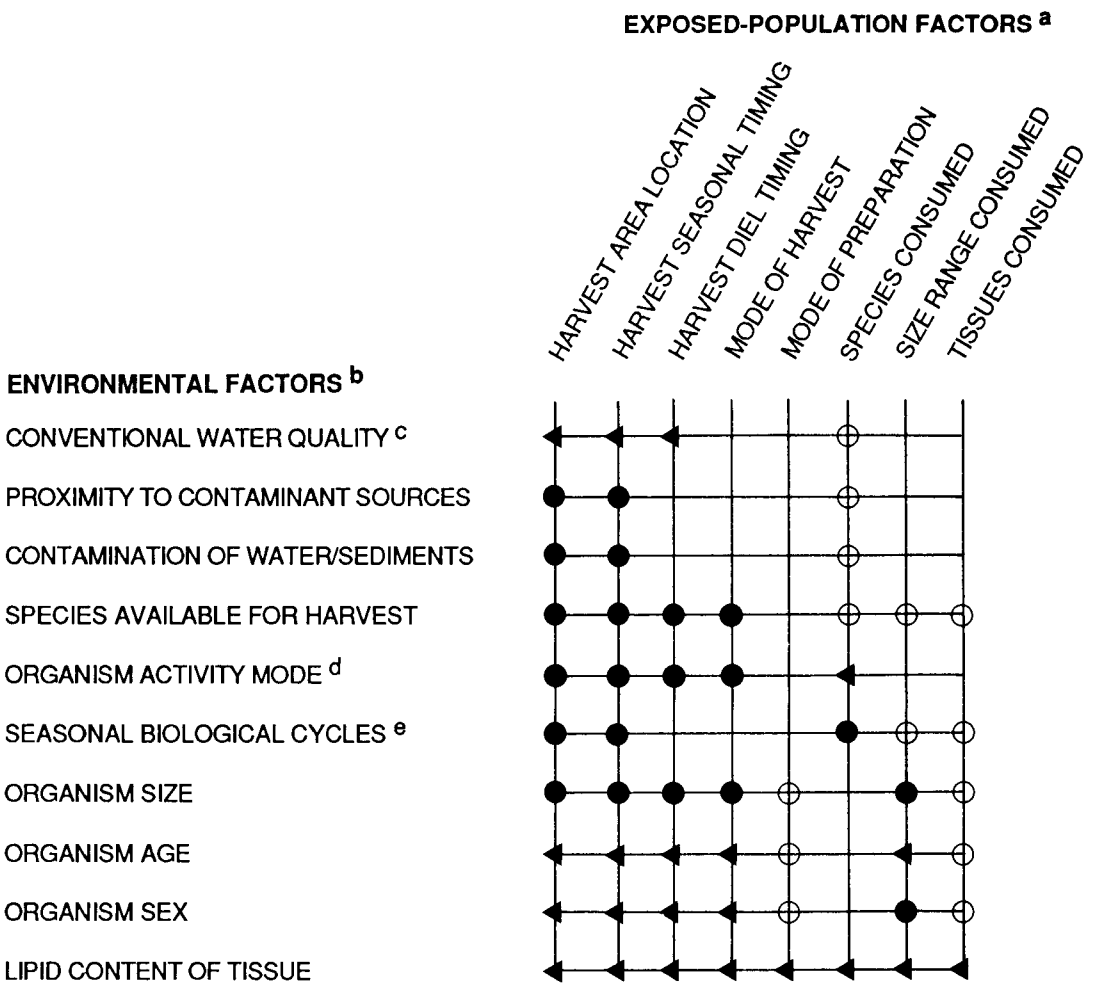
- Conventional water quality (i.e., hardness, salinity, temperature, suspended solids)
- Habitat location, depth, proximity to contaminant sources
- Contaminant concentrations in water
- Contaminant concentrations in sediments
- Species available for harvest, as influenced by habitat, migratory cycles, and fisheries management practices
- Organism activity pattern, food habits, and habitat
- Seasonal biological cycles (e.g., stage of sexual cycle) in relation to the frequency and seasonality of contaminant inputs (e.g., industrial discharges, waste dumps, dredging)
- Organism size (or weight), age, and sex
- Lipid content of tissue analyzed (where lipophilic organic contaminants are of concern).

Examples of the interaction between these factors and parameters of the exposed population are given in Figure 3.

Seasonal variation in environmental factors or activities of the exposed population may correlate with contaminant concentrations in consumed fish and shellfish. Therefore, at least general knowledge of seasonal changes in contaminant concentrations and human consumption patterns may be needed to design an appropriate sampling approach for estimating long-term exposure. Two extreme examples of contamination and diet patterns are provided below:

Homogeneous Diet and Contamination:

- Each of the species is present in the harvest area all year
- There is no seasonal variation in contaminant concentrations
- Contaminant concentrations do not vary among species



[a] Harvest activities and dietary patterns of exposed population:
Mode of harvest refers to fishing technique (e.g., trap,net, or pole)
Mode of preparation refers to trimming and cooking technique
[b] Factors that influence contaminant concentrations in aquatic organisms
[c] Hardness, salinity, temperature, suspended solids
[d] Degree of mobility and contact with sediments
[e] Reproductive, lipid storage, and growth cycles

◀ Population factor affects environmental factor

○ Environmental factor affects population factor

● Mutual interaction between environmental and population factors

Figure 3 Interaction between environmental factors and exposed population factors.

- Species are equally represented in the diet.

Heterogeneous Diet and Contamination:

- Some species are absent from the harvest area during one or more seasons
- Contaminant concentrations vary among species and among seasons
- Some species are eaten more than others, and diet composition varies seasonally.

In the first case above (homogeneous diet and contamination), the study design could be relatively simple. Mean contaminant concentrations could be estimated from analyses of a single composite sample of one of the species collected at one time of year from each harvest area. If previous data were available to verify the lack of variation in chemical concentrations among species and among seasons, it would be appropriate to extrapolate the results from a single composite sample to the entire diet composed of several species. However, this is an unrealistic case. It is more likely that both contaminant concentration and diet composition will vary seasonally, and that contaminant concentrations will vary among species. Analyses of contaminant concentrations in each species during different seasons is generally recommended here to meet the diverse objectives of a typical exposure assessment.

Selection of Target Species and Size Classes

Ideally, the set of species selected for contaminant analysis would include all harvested species. Because available data and funds for collecting new data are often limited, only one or a few target species may be used for human health risk assessment. The particular species selected for an exposure assessment will depend on the study objectives. Examples of approaches and guidance on selection of target species are given below.

Four alternative objectives that affect the choice of target species are:

- Perform a comprehensive analysis of harvested species
- Characterize the typical exposure case represented by the dominant harvested species
- Characterize exposure for the worst-case species (e.g., heavily consumed species expected to be highly contaminated)
- Characterize the spatial distribution of contamination using an indicator species.

The criteria for selecting species for chemical analyses to meet each of these objectives are shown in Table 4. For the first objective (comprehensive species analysis), all of the harvested species do not necessarily need to be analyzed, but some criterion is required to select species for analysis (e.g., the most important species in the harvest that together comprise greater than 95 percent of the catch by weight). For the second objective (typical exposure), a few of the dominant species (by

weight) in the harvest may be selected to represent a typical exposure level. However, this approach has the major disadvantage that highly contaminated species may be overlooked (see **Dominant Harvested Species** below). For the third objective (worst-case species analysis), the target species should be among the most contaminated species in the harvest. If the worst-case assessment is species-specific (i.e., the consumption rate for a single species is used to estimate exposure), then the target species should also be one of the dominant species in the harvest. When the dominant component of the diet differs among subpopulations of concern, then specific dietary information for subpopulations should be used to select the worst-case target species. The target species may be the most contaminated species regardless of its status in the diet of the entire exposed population. For the last objective (site-specific analyses of the spatial distribution of contamination), an indicator species with a small home range that is expected to have high concentrations of contaminants in edible tissue would be selected. Note that an indicator species could be a species that is relatively rare in the harvest. Although home range size and degree of contamination of species may not constrain the selection of species to meet the first two objectives listed above, selecting species without regard to contamination levels will not necessarily ensure that the overall purpose of performing an exposure assessment will be met.

TABLE 4. Criteria for Selecting Target Species[a]

	Alternative Design Objectives[b]			
Species Characteristics	Comprehensive Species Analysis	Typical Exposure Case	Worst-Case Species	Spatial Pattern Indicator Species
Harvest ranking	**Species forming 95% of catch**	**Dominant species in catch**	**Dominant species in catch**	Variable
Home range size	Variable	Variable	Variable	**Small**
Contamination level	Variable	Variable	**High**	**High**

[a] Criteria for selecting target species to meet a given objective are shown in **bold**.
[b] A full statement of each objective is given in the text.

Dominant Harvested Species--If available, data on fisheries catches or consumption from field surveys (e.g., Finch 1973; Puffer et al. 1982; Landolt et al. 1987; McCallum 1985) can be used to select species for analysis that are dominant members of the catch on a wet-weight basis. The advantages of choosing the dominant harvested species for exposure assessment are that:

- Exposure estimates will be based on realistic conditions in terms of relative contribution of species to the diet, providing that catch data reflect consumption patterns or that consumption data are used for the selection of species
- Adequate numbers of organisms for chemical analyses should be relatively easy to obtain.

The disadvantages of this approach are that:

- Species that are minor components of the diet by weight but that are highly contaminated may be overlooked

- Individual humans that consume species other than the dominant component of the diet for the entire exposed population may not be protected when the results of the risk assessment are used in risk management
- Which species are dominant often varies spatially, making it difficult to compare risk estimates for different sites
- Extensive species-specific data on catch, consumption, and contamination patterns are needed to select target species (these data are costly to obtain if not already available)
- If samples are obtained directly from harvesters, a major component of the catch may be unidentifiable because the catch is sometimes cleaned before being surveyed. Moreover, the location of harvest by boat anglers often cannot be verified.

Indicator Species--The use of selected indicator species is an alternative to the use of dominant harvested species. Indicator species can be chosen to represent the average (or maximum) contamination levels in the harvest, as determined from available data or from a pilot survey. Use of indicator species may be appropriate for investigations with multiple objectives (e.g., assessment of bioaccumulation in fishery species and human health risks for specific areas within a water body). Indicator species may include both highly mobile and relatively sedentary species. If small-scale discrimination of spatial patterns of contamination is a concern, indicator species should include nonmigratory biota or species that exhibit minimal movement within the aquatic habitat (e.g., bivalve molluscs and English sole in nearshore marine areas; mussels and sculpins in streams).

The use of a few indicator species for exposure assessment is appropriate for initial screening of geographic areas before more detailed exposure assessments are conducted. If no potential health problems are identified in an initial risk analysis, further data collection may not be warranted, unless long-term monitoring is desired. If, on the other hand, analysis of tissues from indicator species reveals substantial health risks, further field surveys may be needed to perform a detailed exposure assessment. The latter should include data on consumption patterns and contaminant concentrations for a wider variety of harvested species and size classes.

The use of indicator species for exposure assessment offers the following advantages:

- Field surveys based on indicator species are cost-effective because efforts can be focused on collecting large sample sizes of one or a few species rather than minimally adequate sample sizes of many species
- Background information on the distribution, abundance, and contamination of indicator species may be available
- Indicator species can be selected to represent the ayerage or maximum level of contamination expected for all harvested species (assuming background or pilot data are available)

- Because the indicator species does not have to be a dominant species in the harvest, extensive data on catch and consumption patterns may not be needed.

The disadvantages of the indicator species approach are that:

- The exposure estimate may be biased if the indicator species does not truly represent the case of interest (e.g., average- or worst-case concentrations of contaminants)
- The selected species may be a good indicator for some contaminants of concern but not for others
- If the selected indicator species are not major components of the harvest, the exposure assessment may appear unrealistic
- Background data on the distribution, abundance, and contamination of the harvested species are usually needed to select appropriate indicator species
- If a contamination problem is apparent, collection of samples of other species and size ranges of concern may be necessary.

Phillips (1980), Tetra Tech (1985b), and Phillips and Segar (1986) provide criteria for selecting target species for bioaccumulation surveys. Important criteria to consider when choosing indicator species for an exposure assessment are listed below. The target species should be:

- Harvested by the exposed population or be representative of the contamination levels in the primary harvested species
- Representative of a specific study area (e.g., relatively sedentary or restricted from migration by the presence of physical barriers such as dams or waterfalls)
- Easy to sample and abundant enough to obtain adequate samples
- Large enough to yield an adequate sample size for chemical analysis.

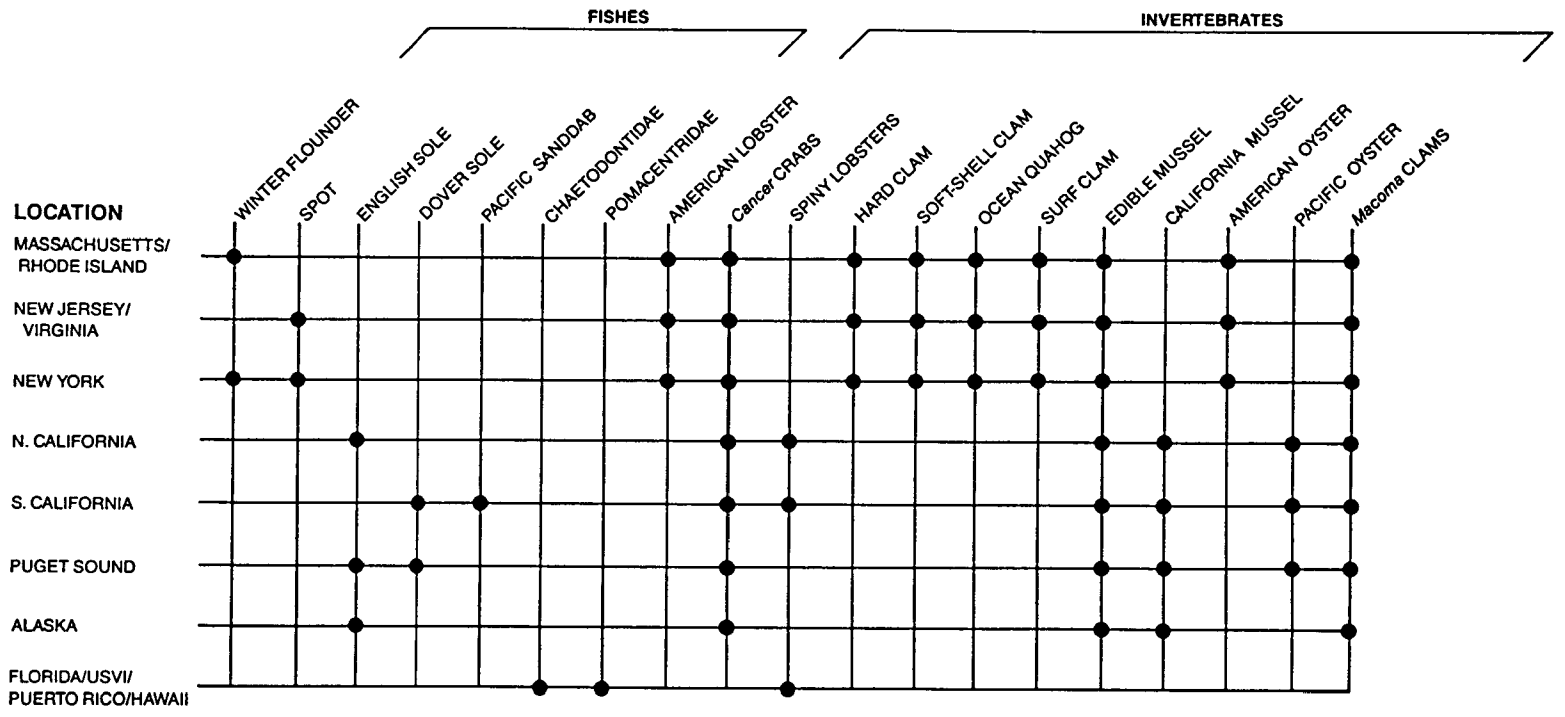
Some additional criteria for target species to be used as indicators of contaminant concentrations in the environment are:

- Contaminant concentrations in the target organisms should be related to those in the environment
- Metabolic regulation of contaminant concentrations by the target species should be absent or weak
- Contaminant interactions should not greatly diminish the usefulness of the target species as a site-specific indicator when contaminant composition is expected to differ among sites
- Target species should integrate the effects of contaminant uptake over time
- Target species should have a high bioaccumulation potential for the contaminants of concern, especially if a worst-case scenario is desired.

A summary of indicator species recommended by Tetra Tech (1985b) for monitoring of chemical residues in tissues of marine and estuarine organisms is shown in Figure 4. Many of the recommended indicator species are associated with soft-sediment substrates. Contact with sediments by such species may lead to body burdens of contaminants that are high relative to those in pelagic organisms of similar lipid content and size. However, the relationship of contaminant concentrations in demersal (bottom-dwelling) vs. pelagic (open-water) organisms is difficult to predict without extensive data. As shown by Tetra Tech (1986c), English sole may be used as an indicator of the order-of-magnitude contaminant concentrations that would be expected in edible tissues of pelagic fish species in Puget Sound, WA. However, relative contamination among species may vary among bays within Puget Sound. For example, in Commencement Bay, the average PCB concentration in muscle of English sole was about twice that in recreationally harvested pelagic species (Pacific cod, Pacific hake, Pacific tomcod, rockfish, walleye pollock, and white-spotted greenling; based on data from Gahler et al. 1982). In Elliott Bay, the average PCB concentration in angler-caught English sole was about 0.4 times that in harvested pelagic species (sablefish, squid, Pacific cod, Pacific hake, Pacific tomcod, rock sole, and rockfish; based on data from Landolt et al.1985). Site-specific data are needed to evaluate contamination of potential indicator species relative to contamination in other species of interest.

Apparently, no comprehensive review of target species for bioaccumulation studies in lakes and streams has been conducted. Salmon and trout (Salmonidae), perch (Percidae), and sunfish (Centrarchidae) species may be preferred for tissue analysis in many cases because they constitute the bulk of the fisheries harvest. However, perch and sunfish species will generally have the lowest concentrations of organic contaminants in edible tissues because of their low lipid content. Freshwater mussels, especially *Anadonta* spp. and *Corbicula* spp., crayfish, sculpins (Cottidae), and catfishes (Ictaluridae) may be preferred as target species for site-specific analyses.

Size Classes--A study design for analysis of chemical residues should incorporate stratified random sampling of a selected size class or various size classes within each target species. Stratification by size is extremely important, since both lipid content and contaminant concentrations can vary greatly among different sized organisms of the same species (Phillips 1980). Moreover, the nature of the relationship between body size and contaminant concentration varies among chemicals, among species, and possibly among sampling stations and seasons (Phillips 1980; Strong and Luoma 1981; Sloan et al. 1985; Johnson 1987). The size classes of each species selected for analysis should be representative of those in the diet of the potentially exposed human population. For persistent chlorinated organic compounds and organic mercury complexes, the largest (i.e., oldest) individuals within an aquatic species are expected to be the most contaminated. If organic compounds are of concern and a limited analysis is planned, the study should focus on the largest individuals likely to be harvested by the exposed human population. If contamination of relatively large individuals is high, sampling and analysis of all size classes typically harvested should be performed to develop specific advisories. For



Reference: Tetra Tech (1985b)

Figure 4 Summary of recommended marine and estuarine indicator species.

example, when contaminant concentrations are positively correlated with fish (or shellfish) size, frequent consumption of the smaller individuals may be acceptable even though consumption of larger individuals should be severely limited.

Sampling Station Locations

Two general approaches to field sampling are possible. First, the investigator can obtain samples directly from harvesters. This approach has the advantage that the sampled population is the population of direct interest for the exposure and risk assessments. However, one drawback of this approach is the potential for contamination or degradation of samples due to handling of the samples by the harvesters. Moreover, the precise sampling locations may be unknown if samples are collected at dockside from recreational or commercial fishing boats. The second approach is to obtain samples independent of the normal harvesting efforts, allowing standard sample handling practices to be implemented. Independent sampling also facilitates the collection of adequate samples for stratification by organism size, habitat, or some other variable. The remainder of this section addresses a sampling effort that is independent of normal harvesting activities.

Sampling stations should generally be located in known harvest areas. However, additional stations in relatively uncontaminated reference or control areas should also be sampled. By comparing results among harvest areas and between each harvest area and the reference station, one can establish not only the degree of spatial heterogeneity but also the magnitude of elevation above reference of contaminant concentrations (and corresponding health risks) at each harvest area. Because sampling depth or vertical position on the shore may influence contaminant concentration in aquatic organisms, reference station characteristics should be closely matched to those for the harvest areas.

Sampling stations may be located within a study area according to one of several probability sampling designs (Figure 5). Gilbert (1987) provides a concise summary of conditions under which each sampling design is preferred.

Simple random sampling implies that each individual organism of a species within a specified area has an equal chance of being selected for measurement and that selection of one individual does not influence selection of others. A simple random sampling strategy is appropriate if there are no major trends or patterns of contamination in the study area. Note that sampling of fish or shellfish with sampling gear (e.g., hook and line, nets) will often be nonrandom with respect to species and size classes because of the selective nature of the gear.

Stratified random sampling involves random sampling within nonoverlapping strata of a population (e.g., subareas where recreational fishing effort is concentrated or where contamination is greatest). This sampling approach is appropriate when localized geographic areas within a harvest region are heterogeneous relative to the kind or degree of contamination.

Two-stage sampling involves random or systematic subsampling of primary units selected by a random sampling technique. For example, fish could initially be collected randomly from a given stream reach. In

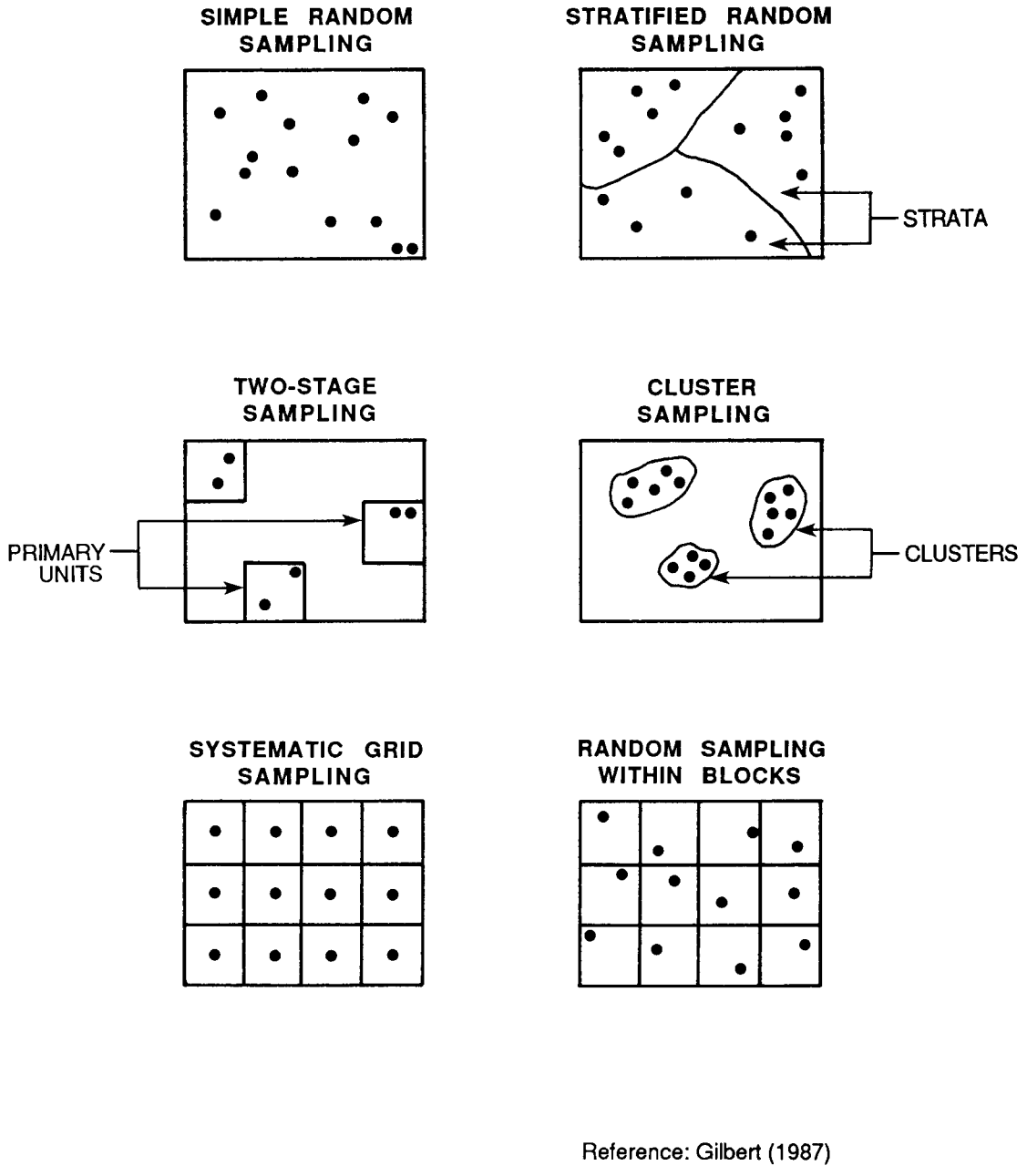


Figure 5 General sampling station layouts for probability sampling in two dimensions.

the second stage of sampling, subsamples of fillet from each fish could be selected randomly for chemical analyses. Multistage sampling is an extension of two-stage sampling.

Cluster sampling involves choosing groups of individual organisms at random, then measuring contaminant concentrations in all individuals within each cluster. Cluster sampling is sometimes used to estimate means if clusters of sampling units (e.g., individual organisms in a clump) can be selected randomly more easily than can individual units.

Systematic sampling consists of sampling at locations and/or times according to a pattern. For example, samples may be collected at equidistant points on a spatial grid or at equally spaced time intervals. Systematic sampling is generally preferred for mapping patterns of contamination. As such, it is more appropriate for soil or sediment sampling than for bioaccumulation studies. The random-sampling-within-blocks strategy shown in Figure 5 combines systematic and random sampling. Such procedures produce more uniform coverage than does simple random sampling.

Gilbert (1987) describes systematic sampling approaches for locating "hot spots" or highly contaminated local areas. He addresses the following questions:

- "What grid spacing is needed to hit a hot spot with specified confidence?"
- "For a given grid spacing, what is the probability of hitting a hot spot of specified size?"
- "What is the probability that a hot spot exists when no hot spots were found by sampling on a grid?"

If grid sampling is to be applied to a bioaccumulation study, the target species must exhibit limited mobility. Grid sampling can also be applied to collection of aquatic sediment samples. Gilbert (1987) provides guidance on spacing of grid samples.

Grid sampling is especially appropriate for identifying environmental contamination associated with discrete sources of pollution such as industrial discharges, storm drains, and combined sewer overflows. The use of caged mussels is a promising approach for identifying sources through chemical residue analysis. As part of the Long Island Sound Estuary Program, EPA Region I is using caged mussels to monitor chemical contaminants entering the Sound from tributaries. The California mussel watch program (e.g., Ladd et al. 1984), the U.S mussel watch (Goldberg et al. 1978, 1983; Farrington et al. 1983), and the NOAA status and trends program (Boehm 1984) illustrate the use of both resident and caged transplant mussels to monitor bioaccumulation of toxic chemicals over space and time. Toxic chemical residues in mussels are excellent indicators of point source discharges as well as pollution gradients (Phillips 1976; Popham et al. 1980; Phelps et al. 1981). U.S. EPA (1982) described recommended protocols for caged mussel studies.

A combination of two-stage and stratified-random (or stratified-grid) sampling is recommended here for most studies of fisheries contamina-

tion to support exposure assessment. The two stages correspond to an individual organism and edible tissue. Samples of individual organisms may or may not be composited depending on specific study objectives (see below, Kinds of Samples, Composite Sampling). Sampling strata may include harvest areas, species, and size classes. Other sampling strategies may be either too simple or inappropriate to meet the typical objectives of exposure assessment studies.

Time of Sampling

The timing of bioaccumulation surveys should be based on the temporal distribution of harvest seasons and inherent biological cycles of target species. The timing of harvest periods depends on the availability of fishery resources, which may be influenced by the migratory patterns and feeding cycles of target species. Biological cycles that influence an organism's susceptibility to bioaccumulation should also be considered when choosing a sampling period. The most important of these is the reproductive cycle, which is discussed further below. In crustaceans (e.g., crab and shrimp), the molting cycle also determines the potential for bioaccumulation of toxic chemicals. The rate of uptake of contaminants by crustaceans is highest just after molting, before hardening of the integument limits its permeability.

The reproductive cycles of aquatic organisms may exert a major influence on tissue concentrations of many contaminants, especially organic compounds (Phillips 1980). If a worst-case analysis is desired, the target species should be sampled at a time during the harvest period when tissue contaminant concentrations are expected to be at their highest levels. In some species, contaminant content of edible tissues may reach a seasonal maximum at or just before the peak of reproductive ripeness, before gametes or offspring are released. This may be especially characteristic of species that are consumed whole (e.g., clams and oysters). In other species (e.g., salmonids), lipid and associated contaminants may be mobilized and transferred from muscle tissue to eggs before they are released. In such species, the peak of contamination may occur in edible tissue (muscle) well before spawning. Because the time of sampling should be tailored to the reproductive characteristics of the target species, sampling periods may vary among species. However, once a sampling period is chosen, it should remain constant over time if an ongoing monitoring program is planned.

An alternative approach is to sample throughout the harvest season for each target species. In this way, representative values can be obtained for estimating means within sampling periods and for detecting seasonal or long-term trends. In most cases, exposure assessments will be performed over relatively short periods of time (e.g., a year), and multiyear sampling may not be required. Within a harvest season, however, sufficient samples should be collected to estimate the mean concentrations of contaminants during the harvest period. To estimate temporal variation or to obtain worst-case estimates, replicate samples will be needed at several times within the harvest season. The frequency of sampling should be related to the expected rate of change in tissue concentrations of contaminants. For an extensive review of temporal changes in bioaccumulation and body burdens of contaminants in aquatic organisms, the reader should consult Phillips (1980).

The kind of tissue sampled and the sampling unit (i.e., individual organisms vs. composites of several organisms) greatly influence the sensitivity, precision, and representativeness of an exposure assessment. The issues of composite sampling and sample preparation techniques are addressed in the following sections.

Composite Sampling--An alternative to the analysis of tissue from individual organisms is the analysis of composite samples. Composite tissue sampling consists of mixing tissue samples, each called a subsample, from two or more individual organisms typically of a single species collected at a particular site and time period. The mixture is then analyzed as a single sample. The analysis of a composite sample therefore provides an estimate of an average tissue concentration for the individual organisms that make up the composite sample. Composite sampling is a cost-effective strategy when the individual chemical analyses are expensive but the cost of collecting individual samples is relatively small. The collection of composite samples is required in cases where the tissue mass of an individual organism is insufficient for the analytical protocol.

Bioaccumulation surveys designed to support exposure assessments may use a composite sampling strategy. Current risk assessment models used by EPA are based on estimates of long-term average exposure. Estimates of the mean concentrations of contaminants in edible tissue samples from harvested organisms are used as estimates of the exposure concentrations for human consumers of fish and shellfish. Composite sampling of the tissue from selected organisms is a method for preparing a sample that will represent an average concentration. The collection of replicate composite tissue samples at specified sampling locations will result in a more efficient estimate of the mean (i.e., the variance of the mean obtained with replicate composite samples is smaller than that obtained with the collection of replicate samples of individual organisms).

One major disadvantage of composite sampling is the inability to directly estimate the range and the variance of the underlying population of individual samples. Such information is extremely useful in bioaccumulation monitoring programs as an early warning signal of increasing levels of contamination. For example, only a few individuals within a sample may contain high contaminant concentrations. Mixing these individuals with less contaminated organisms in a composite sample at a given station may dilute the contaminants and mask a potential problem. In exposure assessment, the patchy distribution of highly contaminated fish or shellfish may indicate the spatial distribution of sources of contaminants.

The benefits of compositing individual samples from a single station within a given sampling period often outweigh the disadvantages just discussed. In such cases, Rohde (1976) and Tetra Tech (1986b) provide a method for calculating the variance of the underlying population (X) of individual samples when the variance of the composite samples (Z) is known:

$$\text{Var } X = n \text{ (Var } Z) \qquad (3)$$

where:

Var X	=	variance of the mean of individual samples from all composites
Var Z	=	variance of the mean of composite samples
n	=	number of subsamples constituting each composite sample.

This equation assumes that replicate observations from individual and composite samples are normally distributed. Also, the composites must each consist of subsamples of equal mass (i.e., the same mass of tissue is taken from each organism). For unequal proportions of composite subsamples (i.e., tissue mass), the variance of the series of composite samples increases and, in extreme cases, exceeds the variance of grab samples. Thus, it is recommended here that the same mass of tissue be taken from each organism contributing to a composite sample of a single species (Tetra Tech 1986b). For the analyses presented below, it was assumed that the composite samples consist of subsamples of equal proportions.

Two special cases of composite sampling are "space-bulking" and "time-bulking" (Phillips and Segar 1986). Space-bulking involves sampling of individual organisms from several locations and combining tissue samples into one or more composite samples for analysis. Time-bulking involves taking multiple samples over time from a single location and compositing these samples. Time-bulking over a harvest season is especially appropriate where short-term variations in contaminant concentrations in tissue samples are significant and budget constraints preclude repeated analyses over time.

The adoption of space-bulking or time-bulking strategies ultimately relates to the objectives of the exposure assessment. Because exposure concentrations are typically averaged over time in risk assessment models, time-bulking may be more justified than space-bulking. In any case, one should use these strategies with extreme caution since significant information on spatial and temporal heterogeneity may be lost. Selection of space-bulking or time-bulking techniques should be supported by analyses of available data or data from preliminary sampling. Tiered analyses of samples can also be used to evaluate the appropriateness of compositing strategies. For example, individual samples may be stored separately over the entire harvest season. At the end of sample collection, preliminary analyses of individual tissue samples from a selected series of sites and times could be performed to evaluate temporal and spatial heterogeneity and to devise an appropriate compositing strategy.

Tetra Tech (1986b) evaluated the effects of composite sampling on the statistical power of a sampling design (see **Appendix D**). Their results demonstrate that the confidence in the estimate of the mean concentration of contaminant in tissue increases as the number of individual samples in the composite increases. The statistical power (i.e., the probability of detecting a specified minimum difference among treatments) increases dramatically with the number of individual samples in each replicate composite sample. However, the increase in power associated with adding more individual samples to each composite

eventually becomes negligible (e.g., at greater than 10 individuals per composite at typical levels of data variability). For moderate levels of variability in chemical residue data, 6 to 10 individual samples within each of 5 replicate composite samples should be adequate to detect a treatment difference equal to 100 percent of the overall mean among treatments. Rohde (1976), Schaeffer et al. (1980), Brumelle et al. (1984), and Gilbert (1987) also discuss statistical aspects of composite sampling.

Sample Preparation--Tissue samples should be removed from target organisms and prepared for analysis according to a well-defined protocol. Tissue preparation methods can greatly affect the results of bioaccumulation analyses (Smith et al. 1973; Skea et al. 1981; Puffer and Gossett 1983; Landolt et al. 1987). In specifying a tissue preparation protocol, the following issues should be addressed:

- Type of tissue (e.g., muscle fillet, whole body, internal organs)
- Location of tissue in organisms' body
- Removal of any or all of shells, scales, skin, and subcutaneous fat
- Raw vs. cooked samples and cooking method
- Homogenization method
- Minimum sample mass for each kind of analysis.

The kind and location of tissue analyzed may influence the realism of the exposure assessment. For example, most humans consume only fillets of fish, not internal organs or whole fish. Because internal organs are often more contaminated by toxic chemicals than are fillets, exposure estimates based on chemical analyses of organs or whole fish could be unrealistically high. Removal of skin and subcutaneous fat from samples before chemical analysis generally reduces the mean concentrations of chlorinated organic compounds. In species with a subcutaneous fat layer, this practice may also reduce the variability of replicate data, allowing more sensitive discrimination among statistical treatments (e.g., species or sampling locations). Within the fillet tissue, contaminant concentrations may vary depending on the original location of the sample on the fish's body.

The effect of cooking on the ultimate health risk from a mixture of chemicals (including any transformation or degradation products produced by heating) is unknown. Some studies have shown decreases in concentrations of lipid-soluble organic compounds such as DDT and PCBs following pan-frying, broiling, or baking of fish fillets (Smith et al. 1973; Skea et al. 1981; Puffer and Gossett 1983). For example, cooking of fillets before chemical analysis may result in a 2 to 65 percent decrease in the concentration of PCBs relative to the uncooked sample, but the results vary greatly with species and cooking method. However, cooking may also activate or transform chemicals to create carcinogens [e.g., formation of benzo(a)pyrene during charbroiling]. Regardless of method of tissue preparation, an adequate mass of each sample and adequate homogenization of samples before they are analyzed are necessary to obtain representative results (e.g., see Tetra Tech 1986e).

Because information on the effects of tissue preparation methods on the results of chemical residue analyses is limited, it is recommended that a pilot survey be performed to establish consistent, reliable methods. Relevant protocols for sample storage and preparation are available in a bioaccumulation monitoring guidance document issued by the EPA Section 301(h) (Clean Water Act) program (Tetra Tech 1986e) and in the EPA *Interim Methods for the Sampling and Analysis of Priority Pollutants in Sediments and Fish Tissue* (U.S. EPA 1981). Because many decisions about sample preparation depend on the specific objectives of the study, no single protocol for sample preparation covers all of the possible approaches. For example, samples are usually blotted dry before being weighed to obtain an estimate of wet weight. However, when bivalve molluscs are being prepared for analysis, it may be desirable to retain excess water for later analysis.

In general, field studies to support exposure assessment should focus on the kind of tissue that is most commonly consumed (e.g., fillet). Analysis of raw edible tissues is recommended to provide data on the concentrations of contaminants initially present in tissues that are normally consumed. Eventually, it may be possible to mathematically account for cooking effects in the exposure assessment. At present, however, data on cooking effects are highly variable.

Sample Replication

Replicated measurements of contaminant concentrations in tissue samples are needed to perform uncertainty analysis (e.g., characterizing the precision of the estimates of mean contaminant concentrations). Replicated data are also needed for many statistical tests of spatial and temporal trends. Sample replication is recommended here for all bioaccumulation measurements to be used in exposure assessments. Guidance on selection of a sample replication scheme is provided in **Appendix E.** In most cases, at least five replicate samples of individual fish (or shellfish) are required to provide minimal statistical power (e.g., ability to discriminate a treatment difference equal to 200 percent of the overall mean among treatments). Increases in sample replication beyond about 10 individual replicates clearly do not provide sufficient benefits in statistical power to justify added costs of sampling and analysis (**Appendix E**). Greater power can be achieved in a cost-effective manner by composite sampling if information on contamination of individual organisms is not needed (**Appendix D**).

Selection of Analytical Detection Limits and Protocols

Criteria for selection of method detection limits for analytical protocols may be based on risk assessment models explained below (see **Risk Characterization**). For example, the analytical chemistry methods may be chosen to enable detection of a chemical concentration associated with a specified minimum risk level defined as acceptable by risk managers. Other factors may dictate choice of a lower detection limit. For example, routine analytical methods may attain much lower limits than required by the specified minimum detectable risk level. Also, lower detection limits may be desired if an objective of the study is to develop baseline bioaccumulation data as well as health risk data. In some cases (e.g., 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, benzidine, dieldrin, N-nitrosodimethylamine), the minimum detection

limit that can be achieved with current technologies corresponds to a plausible-upper-limit risk that is substantially above risk levels of potential concern (e.g., greater than 10^{-5} to 10^{-6}). Tetra Tech (1985c) provides further guidance on detection limits for bioaccumulation surveys.

Approved routine EPA methods for sampling and full-scan analysis of chemical contaminants in tissues are not available. U.S. EPA (1981) published interim methods for sampling and analysis of priority pollutants in tissues. EPA-approved protocols for chemical analysis of water samples were adapted for application to tissue samples as part of the Section 301(h) (Clean Water Act) marine discharge waiver program of the Office of Marine and Estuarine Protection [see Tetra Tech 1986e for 301(h) sampling and analysis protocols]. Specifically, 301(h) analytical methods for extractable organic compounds were adapted from Method 1625 Revision B (U.S. EPA 1984a) and additional guidance from the EPA Contract Laboratory Program for Organic Analysis (U.S. EPA 1984c). When applicable, the 301(h) protocols incorporate established EPA advisory limits for precision, accuracy, and method performance (U.S. EPA 1984c). The EPA Office of Acid Deposition, Environmental Monitoring, and Quality Assurance is developing further guidance on sampling and analysis methods to support exposure assessments.

Other available methods for analysis of chemical contaminants in tissue samples include those used by U.S. FDA (1978), NOAA (MacLeod et al. 1984), and Ozretich and Schroeder (1985). These analytical protocols are designed to apply to specific subsets of the EPA priority pollutants. U.S. FDA (1978) methods, as described in the *Pesticide Analysis Manual*, include variations in procedures for tissues differing in lipid content.

The choice of an analytical protocol may be influenced by available financial resources. Chemical analysis of samples is often the most costly portion of a sampling and analysis program. Higher analytical costs may be required to achieve greater sensitivity (i.e., lower detection limits). Examples of analytical costs are shown in Table 5. At a given level of sensitivity, a wide range of precision is encountered among diverse organic compounds. For example, the low end of the range of variation shown for extractable compounds in Table 5 can usually be achieved for hydrocarbon analyses, whereas substantially more variability is common for analyses of phthalates and some organic acid compounds. A wide range of analytical costs is also encountered at a given level of sensitivity (Table 5). Differences in analytical techniques, laboratory experience with these techniques, and pricing policies of laboratories account largely for the wide variation in cost.

QA/QC Program

An adequate QA/QC program is essential for any sampling and analysis effort to support exposure assessment. U.S. EPA (1984c, 1985c) provides guidance on QA/QC for chemical analysis. Tetra Tech (1986f) describes QA/QC procedures for field and laboratory methods used by the EPA Section 301(h) (Clean Water Act) program. Horwitz et al. (1980) provide guidance on QA/QC in the analysis of foods for trace contaminants. Brown et al. (1985a) describe QA guidelines

followed by NOAA for chemical analysis of aquatic environmental samples.

TABLE 5. Approximate Range of Cost per Sample for Analyses of EPA Priority Pollutants in Tissues as a Function of Detection Limits and Precision[a]

EPA Priority Pollutant Group	Approximate Detection Limit	Typical Precision	Approximate Cost Range[b]
Extractable acid/base/neutrals/ PCBs/pesticides	< 1-20 ppb	< 5% - > 100%	$900 - > $2,000
Volatiles	< 5-20 ppb	< 10% - > 100%	$250 - $350
Metals	100 ppb	< 10% - > 30%	$250 - $300

[a] NOTE: Range of per sample cost is based on multiple quotes compiled for specific applications and 5 samples. The actual costs may vary from the range shown. This information is provided solely for perspective on relative differences in cost and should not be interpreted as a recommendation of appropriate costs for any given circumstance.

[b] Each cost range is mainly the result of laboratory differences in technique and pricing, NOT the range in precision or detection limits shown.

A QA/QC plan should be developed as part of the study design for sampling and analysis of chemical residues. The QA/QC plan should include the following information:

- Project objectives
- Project organization and personnel
- QA objectives for precision, accuracy, and completeness for each kind of measurement
- Summary of sampling procedures, including sample containers, preparation, and preservation
- Forms for documenting sample custody, station locations, sample characteristics, sample analysis request, and sample tracking during laboratory analysis
- Detailed description of analytical methods
- Calibration procedures for chemical measurements
- Internal QC checks for analytical laboratories
- Performance and system audits for sampling and analysis operations
- Preventive maintenance for equipment
- Procedures for data management, data QA review, and data reporting for each kind of measurement
- Corrective actions

- Procedures for QA/QC reporting and responsible federal and state QA officers
- Mechanisms for approval of alterations to the monitoring program, for suspending sample analyses, and for stopping sample analyses within a tiered design.

Relevant portions of the QA plan should be incorporated in the statement of work for each contract laboratory involved in sample analyses.

Documentation and QA Review of Chemical Data

Adequate documentation of the results of chemical analyses are needed to ensure proper interpretation of the data. If a contract laboratory is performing the sample analyses, such documentation should be specified in the original statement of work. The documentation listed below is recommended for chemical residue data:

- A cover letter discussing analytical problems (if any) and referencing or describing the procedure used
- Reconstructed ion chromatograms for each sample analyzed by gas chromatography/mass spectrometry (GC/MS)
- Mass spectra of detected target compounds for each sample analyzed by GC/MS
- Chromatograms for each sample analyzed by gas chromatography/electron capture detection (GC/ECD) and/or gas chromatography/flame ionization detection (GC/FID)
- Raw data quantification reports for each sample
- A calibration data summary reporting calibration range used [and decafluorotriphenylphosphine (DFTPP) and bromofluorobenzene (BFB) spectra and quantification report for GC/MS analyses]
- Final dilution volumes, sample size, wet-to-dry ratios, and instrument detection limit
- Analyte concentrations with reporting units identified (to two significant figures unless otherwise justified)
- Quantification of all analytes in method blanks (ng/sample)
- Method blanks associated with each sample
- Tentatively identified compounds (if requested) and methods of quantification (include spectra)
- Recovery assessments and a replicate sample summary (laboratories should report all surrogate spike recovery data for each sample; a statement of the range of recoveries should be included in reports using these data)
- Data qualification codes and their definitions.

The data reporting forms for the EPA Contract Laboratory Program illustrate an appropriate format for documentation of chemical data.

All contaminant concentration data to be used in a risk assessment should undergo a thorough QA review by a qualified chemist independent of the laboratory that analyzed the samples. In some cases, the analytical laboratory may provide a QA review that is simply checked by an independent chemist. The purpose of the QA review is to evaluate the data relative to data quality objectives (e.g., precision and accuracy) and performance limits established in the QA plan. In many cases, qualifiers are necessary for selected data values. These qualifiers should be added to the database. A summary of data limitations should always be included in the risk characterization (see below, Risk Characterization). The EPA Office of Acid Deposition, Environmental Monitoring, and Quality Assurance is developing guidelines for quality assurance of chemical data to support exposure assessments.

Statistical Treatment of Data

Statistical analyses of data will depend on specific study objectives. For each species, statistical summaries of tissue concentration data should include sample size, estimates of arithmetic mean concentration, range, and a measure of variance (standard error or 95 percent confidence limits). Geometric mean concentrations are appropriate measures of central tendency when only estimates of tissue burden of contaminants or exposure dose are desired. However, arithmetic means are needed to compare exposure estimates with RfDs and to calculate health risk for chronic effects because long-term consumption is an averaging process. Mean tissue concentrations and variances may be calculated for mixed-species diets if data are available on the proportion of each species in the diet.

The one-way ANOVA model discussed earlier or multifactor ANOVA models are appropriate for testing for differences in mean contaminant concentrations among species, among sampling stations, or among time periods (Schmitt 1981; also see Tetra Tech 1986b,d). For small sample sizes and data that do not satisfy the assumptions of ANOVA, nonparametric tests such as the Wilcoxon rank sum test for two treatments or the Kruskal-Wallis test for multiple comparisons are recommended. These tests have the added advantage of being relatively insensitive to a few missing data points or undetected observations (Gilbert 1987). Long-term data sets may be tested for trends by time series analysis (for reviews, see Montgomery and Reckhow 1984 and Gilbert 1987). Examples of trend analysis for chemical contaminants in fish are provided by Brown et al. (1985b) for PCBs in striped bass of the Hudson River and by DeVault et al. (1986) for PCBs and DDT in lake trout from the upper Great Lakes.

Data on concentrations of contaminants of concern in tissue samples will often contain observations below detection limits. Means and variances for tissue concentrations should be calculated twice: once using detection limits for undetected observations and once using 0 for undetected observations. Although alternative approaches are possible (e.g., using one-half the detection limit), the approach recommended here yields more accurate, complete results by quantifying the range of the estimated values. According to the EPA Exposure Assessment Group, calculations of plausible-upper-limit risk estimates based on detection limits should generally be avoided. However, risk estimates based on detection limits may occasionally be useful to indicate that particular chemicals, species, or geographic locations are not

problems, even assuming undetected contaminants are present at concentrations just below their respective detection limits.

The choice of contaminant concentration values to use in subsequent calculations to estimate exposure (and ultimately risk) is partly a risk management decision. Exposure estimates are commonly based on arithmetic mean concentrations of contaminants in edible tissue of fish or shellfish. Use of the upper 90 or 95 percent confidence limit in place of the mean would provide a conservatively high estimate of exposure. Calculation of conservative estimates for exposure is an appropriate step in uncertainty analysis. However, U.S. EPA (1986b) guidelines on exposure assessment discourage the use of worst-case assessments. Use of upper confidence limits for chemical concentrations in combination with a plausible-upper-limit estimate for the Carcinogenic Potency Factor may lead to an unrealistic (i.e., highly unlikely) estimate of upper-bound risk, especially if a conservatively high estimate of fish consumption is also adopted. In most cases, the best estimate of exposure based on mean contaminant concentrations should be used to develop risk estimates. If upper confidence limits for chemical concentrations are used to develop risk estimates, the effects of compounding conservative assumptions should be evaluated.

Analysis of Sources, Transport, and Fate of Contaminants

Exposure pathways and routes are potential mechanisms for transfer of contaminants from a source to a target human population or subpopulation. The sources, transport, and fate of chemicals in the environment are analyzed to evaluate exposure pathways and routes. To compensate for a limited database, this analysis often includes mathematical modeling of contaminant transport and fate. The modeling of exposure pathways focuses on transfer of contaminants from source to target fishery species, since the transfer step from fishery to humans can be based on knowledge of fishery harvest activities (see below, **Exposed Population Analysis**). When extensive data on contamination of a fishery is available and source-tracing is not an objective, modeling of chemical transport and fate may be unnecessary.

Although the specific uses of modeling in exposure assessment are diverse, several broad objectives may be outlined as follows:

- Estimate the spatial and temporal distribution of concentrations of chemical contaminants in edible tissues of fish and shellfish
- Identify potential sources of contaminants
- Evaluate alternative source controls or remedial actions.

Estimation of contaminant concentrations in fish and shellfish by mathematical modeling is especially useful when available data on tissue contaminants are limited. If the distribution of contaminants in sediments or water can be estimated from available data or model predictions, estimates of chemical residues in fishery species can be based on relationships of tissue contamination to environmental con-

tamination (e.g., laboratory-derived BCFs). Spatial characterization is important for identifying areas of high contamination resulting from heterogeneous transport and deposition of contaminants. Temporal characterization is important for defining time-dependent changes in contaminant concentrations that may mitigate future exposure and risk.

Predictions of spatial trends in chemical residues may also aid in identifying and controlling sources of pollutants. For example, when data on sources, sediments, and tissues are available, modeling of chemical transport and transformation processes may help to link the patterns of chemical contaminants observed in the environment with specific individual sources. Information on differential degradation of contaminants and compositional relationships for complex mixtures can be used to support the model analysis (e.g., calibration and validation). Finally, modeling of contaminant releases in combination with chemical residues in fisheries may aid in evaluating alternative source controls or remedial actions for waste sites. The results of modeling can indicate the level of source control or remedial action needed to achieve a desired level of environmental quality.

In the exposure assessment guidelines, U.S. EPA (1986b) describes general approaches for characterizing sources, exposure pathways, and environmental fate of chemicals. Analysis of chemical transport and fate is a major endeavor, which cannot be addressed in detail here. For additional information, the interested reader should consult Callahan et al. (1979), Burns et al. (1981), Jensen et al. (1982), Mills et al. (1983), Games (1983), Connor (1984b), Thomann and Connolly (1984), Onishi (1985a,b), U.S. EPA (1986b), Pastorok (1986), and references therein.

Analysis of Exposed Populations

The second stage of the exposure assessment, analysis of exposed populations, includes the following steps:

- Identify potentially exposed human populations and map locations of fisheries harvest areas
- Characterize potentially exposed populations
  - Subpopulations by age, sex, and ethnic composition
  - Population abundance by subpopulation
- Analyze population activities
  - Harvest trip frequency
  - Seasonal and diel patterns of harvest trips
  - Time per harvest trip
  - General activity (e.g., clamming, crabbing, fishing)
- Analyze catch/consumption patterns by total exposed population and subpopulation
  - -Proportion of successful trips
  - Catch by numbers and weight according to species
  - Time since last meal of locally harvested organisms
  - Number of consumers sharing catch
  - Parts of organisms eaten
  - Method of food preparation (e.g., raw, broiled, baked)

- Estimate arithmetic average consumption rate by species and by total catch for the total exposed population and for subpopulations. For seasonal fisheries, consumption rates may be estimated on an annual and a seasonal basis.

Only selected steps may be performed in a given exposure assessment, depending on data availability, study objectives, and funding limitations. Note that many of the steps to characterize harvest activities and consumption rates apply only to analyses of recreational fisheries. When estimating consumption of fish and shellfish of commercial origin, harvest activities are irrelevant. Also, the specific geographic origin of commercial fisheries products is often unknown.

Two approaches to estimating consumption rates are outlined below. In the first approach, a comprehensive analysis of a recreational fishery is performed based on extensive catch/consumption data for the exposed population. In the second approach, estimates of consumption rates are based on available values for the U.S. population (or subpopulations) or other assumed values. Most of the available estimates were derived from recall or diary studies (Lindsay 1986) and include commercial fisheries products. It is recommended here that local or regional assessments of fishery consumption be performed whenever possible to avoid possible errors inherent in extrapolating standard values for the U.S. population to distinct subpopulations. Moreover, extrapolation of standard consumption estimates that include commercial fisheries products to recreational fisheries should generally be avoided.

In developing a profile of the exposed population, there is no single "correct" estimate of consumption rate. Because consumption rates are highly variable, use of a range of values or a probability distribution for consumption rate estimates is recommended. This approach may also be followed when estimating consumption rates for subpopulations of interest.

An alternative to the typical practice of basing risk estimates on selected consumption rates involves presenting risk estimates graphically for a wide range of consumption rates that essentially includes all possible realistic values (see below, **Presentation and Interpretation of Results**). For example, plots of estimated risk vs. consumption rate may be useful for public presentations on recreational fishery resources. In this case, the risk associated with any particular subgroup within the exposed population may be evaluated by selecting a consumption value for the subgroup and reading the corresponding risk from the graphic plot. Use of this approach avoids having to collect extensive data on the exposed population. A similar approach involves selecting an "acceptable" (tolerable) risk level and providing advice on levels of consumption, such that the "acceptable" risk is not exceeded. The advantage of both of these approaches is that consumption rates need not be determined or assumed.

Comprehensive Catch/Consumption Analysis

Appropriate field survey forms, data analyses, and format for presentation of results for a comprehensive catch/consumption analysis of

fisheries are provided by Landolt et al. (1985), McCallum (1985), and National Marine Fisheries Service (1986). Details of methods will not be presented here, except to emphasize some important considerations for calculating consumption rates. Examples of analyses of catch/consumption data can be found in Puffer et al. (1982) for coastal waters of southern California, in Landolt et al. (1985, 1987) for Puget Sound, in Belton et al. (1986) for New York Bay and Newark Bay, and in National Marine Fisheries Service (1986) and companion documents for other areas of the U.S.

Lindsay (1986) reviewed alternatives to field survey methods, including use of food diaries and dietary recall. Gartrell et al. (1986a,b) described methods used by FDA in their total diet studies to estimate rates of consumption of various foods. Note that the results of the FDA total diet studies are of limited use in the present context because fish are grouped with meat and poultry. Estimates of seafood consumption used by FDA to calculate average intake of methylmercury for exposed portions of the U.S. population were based on a diary survey sponsored by the Tuna Research Foundation (Tollefson and Cordle 1986). Supplementary information on analysis of fisheries consumption data can be found in SRI (1980).

The average rate of consumption of fish or shellfish is the key exposure variable for use in subsequent steps of risk assessment. Consumption rates should be expressed in terms of g/day and meals/year [meals/year may be calculated from g/day by assuming an average meal of fish or shellfish equals about 150 g (0.33lb) if the average meal size is unknown]. Average consumption rate for each harvest species is calculated from field data according to the following steps:

- For each successful angler trip, calculate the weight of harvest by species based on number and total weight harvested per household
- Calculate mean harvest weight consumed per person per time by:
  - Dividing the total harvest weight for each species by the number of consumers in household and by the days elapsed since last meal from the same area
  - Multiplying the value obtained in the preceding computation by a factor to account for the proportion of cleaned weight to total weight [according to Landolt et al. (1985), this factor equals about 0.5 for squid and crabs, 0.3 for fish, and 1.0 for shucked clams; these estimates should be verified or replaced by local data]
- Calculate mean consumption rate per person by geographic harvest area, by subpopulation, and by total exposed population.

Note that the above method (cf. Landolt et al. 1985, 1987) may provide a biased estimate of average consumption rate due to its dependence on a short-term observation (i.e., time since last meal). Averaging of data over a longer time period might be preferable, but such data may be more susceptible to biases from inaccurate recall of consumers (interviewees). Harvest weights should generally be determined directly rather than from length measurements. However, for shellfish and

crabs, it may be necessary to establish tissue weights from weight-length regression analysis.

The model for calculating mean daily consumption rate (I_{ijk}) for fishery species i, human subpopulation j, and area k is therefore:

$$I_{ijk} = \frac{1}{N_{ijk}} \sum_{1} I_{ijkl} = \frac{1}{N_{ijk}} \sum_{1} \frac{w_{ijkl} p_i}{H_{jkl} T_{jkl}} \quad (4)$$

where:

I_{ijkl} = Mean daily consumption rate of species i for subpopulation j, area k, and household l (kg/day)

N_{ijk} = Number of households (successful harvest trips) for species i, subpopulation j, and area k

w_{ijkl} = Weight of species i harvested by household l of subpopulation j in area k (kg)

p_i = Proportion of cleaned edible weight of species i to total harvested weight

H_{jkl} = Number of people in household l of subpopulation j in area k

T_{jkl} = Time elapsed since last meal by household l of subpopulation j in area k (days).

When consumption rates (I_{ijkl}) are log-normally distributed, a geometric mean consumption rate may be calculated by log-transforming the data before applying Equation 4 to calculate a mean consumption rate.

Consumption rate data may be summarized further by calculating means across species, subpopulations, and areas. However, it should be recognized that means of I_{ijk} across species do not represent actual diet patterns for consumers of mixed-species diets. To calculate mean consumption rates for mixed-species diets, all I_{ijkl} should be summed across species within a household before determining mean consumption rates across households (I_{jk}):

$$I_{jk} = \sum_{1} \frac{I_{jkl}}{N_{jk}} = \sum_{1} \sum_{i} \frac{I_{ijkl}}{N_{ijk}} \quad (5)$$

where:

I_{jkl} = Mean daily consumption rate of all fishery species for household l, subpopulation j, and area k (kg/day)

N_{jk} = Number of households in subpopulation j and area k

and other terms are defined above.

Landolt et al.(1985) summarized the assumptions involved in calculating mean consumption rates (I_{ijkl}) by household as follows:

- Consumption
  - p_i values are assumed as noted above
  - Catch was distributed evenly among consumers in household
  - People in household actually ate the entire cleaned catch

- Personal harvest consumption was distributed evenly over the time interval since the last successful trip

- Fishing interval
  - Fishing frequency (days) is related to seasonal fisheries; that is, interviewees did not report average time interval for entire year but only for recent past. Therefore, calculated consumption rates cannot be directly extrapolated to a yearly basis. Fishing interval was set to 1 day if unreported (Landolt et al. 1985).

Despite the limitation noted in the last item above, calculated consumption rates can be extrapolated to an annual average rate by multiplying the I_{ijkl} by 365 days and by a species-specific factor equal to the fraction of the year a fishery is available. Determination of this species-specific factor is somewhat subjective because of large seasonal fluctuations of the harvest (e.g., Appendix E of Landolt et al. 1985). These factors should be determined on a case-specific basis.

Assumed Consumption Rate

In many cases, comprehensive data on fisheries catch and consumption patterns are not available. For some risk assessment problems (e.g., ranking of potential problem chemicals in aquatic organisms or development of consumption advisories) extensive catch/consumption data are not needed. Moreover, catch/consumption patterns undoubtedly vary over time. Extensive long-term monitoring of catch/consumption for all areas of interest within a large water body may not be warranted. Despite its obvious limitations, extrapolating consumption data from one area (or time) to another may be a suitable approach when:

- Site-specific data are unavailable
- Differences among areas (or times) are expected to be small
- Precise estimation of average fish or shellfish consumption is unnecessary to meet the study objectives.

In the past, many risk analysts have simply assumed standard values for food consumption rates based on previous analyses of dietary patterns of the U.S. population (U.S. EPA 1980b; SRI 1980). Average values for fish and shellfish consumption for the U.S. population generally range from 6.5 to 20.4 g/day (Nash 1971; National Marine Fisheries Service 1976, 1984; SRI 1980; U.S. Department of Agriculture (USDA) 1984; also see **Appendix F**). Most estimates include fish and shellfish (molluscs, crustaceans) in marine, estuarine, and fresh waters, but saltwater species form the bulk of consumed items. Most estimates also include commercially harvested fisheries products. Also, estimates of average U.S. consumption do not account for subpopulations in areas such as the Great Lakes that consume large quantities (20 g/day) of locally caught sport fish.

An estimate of 6.5 g/day for consumption of commercially and recreationally harvested fish and shellfish from estuarine and fresh waters was used by U.S. EPA (1980b) to develop water quality criteria based on human health guidelines. The value of 6.5 g/day is an average per-capita consumption rate for the U.S. population, including non-

consumers, based on data in SRI (1980). Consumption rates for portions of the U.S. population (e.g., by region, age, race, and sex) show that average consumption of fisheries organisms may vary from about 6 to 100 g/day (e.g., Suta 1978; SRI 1980; Puffer et al. 1982). Finch (1973) determined that approximately 0.1 percent (i.e., the 99.9th percentile) of the U.S. population consumes 165g/day of commercially harvested fish and shellfish. Pao et al. (1982) provided estimates of 48 g/day for the average and 128 g/day for the 95th percentile consumption rates by U.S. consumers of fish and shellfish. Rupp (1980) presented estimates of average daily consumption of freshwater fish, saltwater fish, and all shellfish according to age group within the U.S. population. SRI (1980) presents average and 95th percentile rates of consumption of all fish and shellfish according to age group, race, region and other demographic variables. Estimates of food consumption rates for specific subpopulations in the U.S. are also available from a database maintained by the EPA Office of Pesticide Programs (see Appendix F). Limitations of fisheries consumption data are discussed by SRI (1980) and Landolt et al. (1985). The present status of data on fish consumption in the U.S. is also reviewed by Wagstaff et al. (1986).

One or more of the following values of average consumption rate may be assumed when site-specific data are unavailable:

- 6.5 g/day to represent an estimate of average consumption of fish and shellfish from estuarine and fresh waters by the U.S.population (U.S. EPA 1980b)
- 20 g/day to represent an estimate of the average consumption of fish and shellfish from marine, estuarine, and fresh waters by the U.S. population (USDA 1984)
- 165 g/day to represent average consumption of fish and shellfish from marine, estuarine, and fresh waters by the 99.9th percentile of the U.S.population (Finch 1973)
- 180 g/day to represent a "reasonable worst case" based on the assumption that some individuals would consume fish at a rate equal to the combined consumption of red meat, poultry, fish, and shellfish in the U.S. (EPA Risk Assessment Council assumption based on data from the USDA Nationwide Food Consumption Survey of 1977-1978; see Appendix F).

Extrapolation of these values to local populations and recreational fisheries should generally be avoided. Limited estimates of average consumption rates for recreational fisheries are given in SRI (1980). Whenever possible, data on local consumption patterns should be collected or obtained from a current database. Alternatively, risk estimates may be expressed on a unit consumption basis (i.e., per unit weight of fish/shellfish consumed). This latter approach is used by some states in issuing sportfishing advisories. If average consumption values listed above are assumed for local risk assessment, it is recommended that a range of values be used. The references cited earlier should be consulted for consumption rate data for fish and shellfish separately, or for individual species (also see references cited in **Appendix F**).

Exposure Dose Determination

In the next step of the exposure analysis, information on estimated contaminant concentrations and rate of consumption of fish and shellfish are combined to estimate chemical intake by exposed humans. Analyses of single-species diets and mixed-species diets are discussed separately in the following sections.

Single-Species Diets

The general model to calculate chemical intake for a single-species diet is:

$$E_{ijkm} = \frac{C_{ikm} I_{ijk} X_m}{W} \quad (6)$$

where:

- E_{ijkm} = Effective ingested dose of chemical m from fishery species i for human subpopulation j in area k (mg kg^{-1} day^{-1} averaged over a 70-year lifetime)
- C_{ikm} = Concentration of chemical m in edible portion of species i in area k (mg/kg)
- I_{ijk} = Mean daily consumption rate of species i by subpopulation j in area k (kg/day averaged over 70-year lifetime)
- X_m = Relative absorption coefficient, or the ratio of human absorption efficiency to test-animal absorption efficiency for chemical m (dimensionless)
- W = Average human weight (kg).

Values of subscripted terms above may be estimated means or uncertainty interval bounds (e.g., 95 percent confidence intervals) depending on the exposure scenario being modeled (e.g., worst case vs. average case vs. lower-limit case). Note that E_{ijkm} is analogous to the dose "d" in Equations 1 and 2. The term "effective" ingested dose (E_{ijkm}) is introduced to emphasize that estimates of chemical intake (i.e., ingested dose) may be modified by the term X_m to account for differential absorption of contaminants by humans and bioassay animals.

Absorption coefficients (X_m) are assumed equal to 1.0 unless data for absorbed dose in animal bioassays used to determine toxicological indices (carcinogenic potency or RfD) are available and the human absorption coefficient differs from that of the animal used in the bioassay. Assuming that X_m is equal to 1.0 is equivalent to assuming that the human absorption efficiency is equal to that of the animal used in the bioassay. In the absence of data to the contrary, this is appropriate. Toxicological indices are determined from bioassays that usually measure administered (ingested) dose. Therefore, the estimated chemical intake by humans, E_{ijkm}, is usually the ingested dose, not the absorbed dose. If the toxicological index used to estimate risk is based on the absorbed dose, then an estimate of human absorption efficiency for the chemical of concern may take the place of the term X_m in Equation 6 above. In most cases, however, information or

assumptions about absorption efficiencies has been incorporated into EPA's estimates of RfDs and Carcinogenic Potency Factors. Therefore, X_m is usually dropped from Equation 6 and E_{ijkm} becomes simply the ingested dose.

W is usually assumed to be 70 kg for the "reference man" (U.S. EPA 1980b). Assuming other average values to account for growth from a child's body weight to adult weight over a lifetime would not change the results of carcinogen risk assessment substantially. Concerns about exposures over a time period of less than about 15 years may require modeling of early childhood exposures. Standard values for age-specific body weight and other factors used in exposure assessment are provided by Anderson et al. (1985).

Mixed-Species Diets

Estimation of chemical exposure due to a mixed-species diet is complicated by variation in the dietary habits of individuals. The various diets of individual humans may differ from one another in the kinds and relative proportions of fishery species consumed. The sum of species-specific exposures (E_{ijkm}) is not equivalent to total exposure for a mixed-species diet. In a diverse fishery, each individual consumer is likely to consume only a subset of the total available species. Thus, the sum of species-specific exposures might overestimate the average consumption rate for mixed-species diets.

To estimate average chemical exposure resulting from a mixed-species diet, an exposure dose should first be estimated for each individual in a subpopulation as follows:

$$E_{hjkm} = \sum_{i} \frac{C_{ikm} I_{hijk} X_m}{W} \qquad (7)$$

where:

E_{hjkm} = Effective exposure dose of chemical m from a mixed-species diet eaten by individual human h in subpopulation j in area k (mg kg^{-1} day^{-1} averaged over a 70-year lifetime)

I_{hijk} = Average consumption rate of species i by individual h in subpopulation j in area k (kg/day averaged over a 70-year lifetime)

and other terms are defined as above. The average exposure dose for mixed species diets is:

$$E_{jkm} = \frac{\sum_{h} E_{hjkm}}{H_{jk}} \qquad (8)$$

where:

E_{jkm} = Average effective exposure dose of chemical m from mixed-species diet for subpopulation j in area k (mg kg^{-1} day^{-1})

H_{jk} = Number of persons in subpopulation j in area k.

Uncertainty estimates can be obtained by calculating 95 percent confidence limits for E_{jkm}.

References to protocols for sampling and analysis of toxic chemical residues in fish and shellfish are provided above (see **Measurement of Contaminants**). For the updated status of protocols and new developments, contact a representative of the EPA Office of Water (**Appendix A**) or one of the EPA Office of Research and Development Laboratories (**Appendix G**). Information on sampling and analysis of commercial fisheries products collected from the marketplace is available in FDA Compliance Program Guidance Manuals (available from FDA, Freedom of Information (HFI-35), 5600 Fishers Lane, Rockville, MD 20857).

Compilations of data on concentrations of chemical contaminants in fish and shellfish are available in the EPA Ocean Data Evaluation System (ODES), reports of the NOAA Status and Trends Program (e.g., Matta et al. 1986), Tetra Tech (1985b), and Capuzzo et al. (1987). For current local information, contact a member of the EPA Regional Network for Risk Assessment/Risk Management Issues (**Appendix H**). Many state health and environmental agencies maintain regional databases on chemical residues in fish and shellfish. For example, the New York State Department of Environmental Conservation and the New Jersey Department of Environmental Protection publish periodic reports on contaminants levels in fish (e.g., Armstrong and Sloan 1980; Belton et al. 1986; Sloan and Horn 1986). The Wisconsin Department of Natural Resources (Bureau of Water Quality) maintains computerized records of long-term data on PCB concentrations in fish of the Great Lakes.

Summaries of data on contaminant concentrations in a variety of foods are available in Grasso and O'Hare (1976), Lo and Sandi (1978), Stich (1982), U.S. FDA (1982), and Vaessen et al. (1984). FDA is developing a data system called FOODCONTAM for pesticide and industrial contaminant residues in foods.

References containing estimates of the rates of consumption of fish and shellfish by the U.S. population were presented above (see **Assumed Consumption Rate**). The EPA Office of Pesticide Programs maintains the Tolerance Assessment System (Saunders and Petersen 1987). The Tolerance Assessment System uses a USDA database (based on a 1977-1978 survey) to generate estimates of consumption of various foods stratified by specific subpopulations (e.g., infants, children, and adults in the northeastern U.S.). The Office of Pesticide Programs is also developing information on the effects of food preparation methods on chemical residues in food.

Risk Characterization

In the risk characterization stage, results of the hazard, exposure and the dose-response assessments are combined to estimate the probability and extent of adverse effects associated with consumption of contaminated fish or shellfish. An overview of the risk characterization process is shown in Figure 6. In human health risk assessment, carcinogens and noncarcinogens are treated separately. Indices of risk for these different categories of toxicants are based on different dose-response models (see above, **Dose-Response Assessment**).

The procedures for generating quantitative estimates of risk are emphasized in the following sections. However, it is critical that numerical estimates of risk not be presented in isolation from the assumptions and uncertainties inherent in the process of risk assessment. The risk characterization should include a discussion of assumptions and uncertainties and their potential impact on numerical estimates of risk; i.e., the degree to which the numerical estimates are likely to reflect the actual magnitude of risk to humans. For example, if upper confidence limits for mean chemical concentrations are used to develop risk estimates, the effects of compounding assumptions of upper-bound estimates of carcinogenic potency and conservatively high estimates of consumption rate should be evaluated. A risk characterization should include a summary of the preceding steps of the risk assessment: hazard assessment, dose-response assessment, and exposure assessment. The weight-of-evidence classification and other supporting information should be summarized concisely. Approaches to presentation of summary information to be included in risk characterization are presented in the next chapter (see below, **Presentation and Interpretation of Results**).

Carcinogenic Risk

Numerical estimates of carcinogenic risk can be presented in one or more of the following ways (U.S. EPA 1986a):

- **Unit risk:** The excess lifetime risk corresponding to a continuous constant lifetime exposure to a unit carcinogen con-

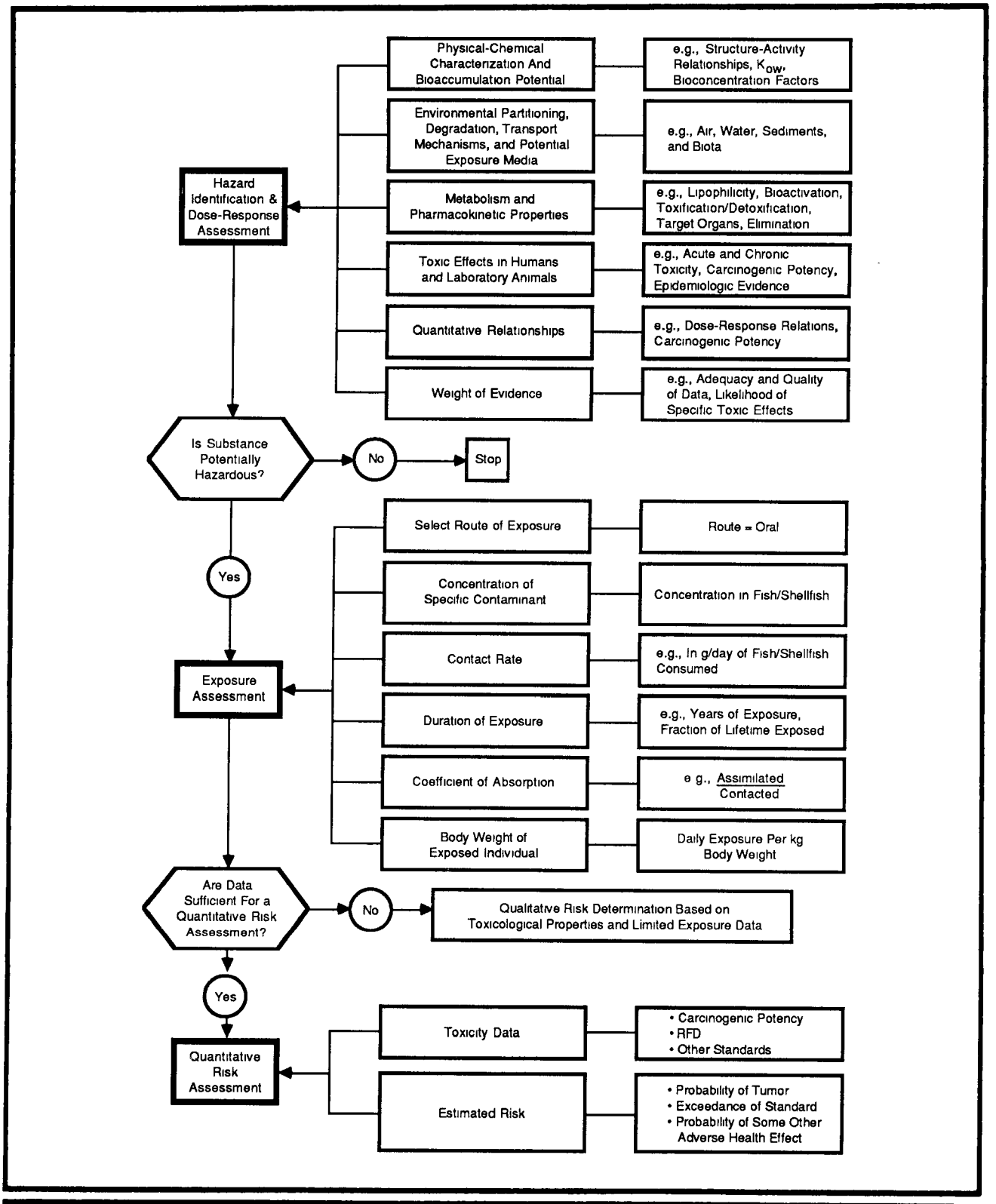


Figure 6 Conceptual structure of quantitative health risk assessment model.

centration (e.g., 1 mg/kg carcinogen in edible tissue of fish or shellfish)

- **Dose or concentration corresponding to a specified level of risk**: For example, a guideline for maximum allowable contamination of a specified medium may be derived from a maximum allowable risk value established by risk managers
- **Individual and population risks**: Upper-limit estimates of excess lifetime cancer risk may be expressed for individuals (as a probability estimate) or for the exposed population (as an estimate of the number of cancers produced within a population of specified size per generation).

Regardless of the option chosen for expressing risk, final numerical estimates should be presented as one significant digit only, followed by the EPA classification of the weight of evidence for carcinogenicity in brackets (U.S. EPA 1986a).

The general model for estimating a plausible upper limit to excess lifetime risk of cancer at low doses for a single-species diet is:

$$R^*_{ijkm} = q_1{}^*_m \, E_{ijkm} \qquad (9)$$

where:

R^*_{ijkm} = Plausible-upper-limit risk of cancer associated with chemical m in fishery species i for human subpopulation j in area k (dimensionless)

$q_1{}^*_m$ = Carcinogenic Potency Factor for chemical m [$(mg\ kg^{-1}\ day^{-1})^{-1}$] estimated as the upper 95 percent confidence limit of the slope of a linear dose-response curve

E_{ijkm} = Exposure dose of chemical m from species i for subpopulation j in area k ($mg\ kg^{-1}\ day^{-1}$).

The actual risk is likely to be below the estimated upper-limit value calculated from Equation 9, and may be zero in some instances. Equation 9 corresponds to Equation 2 above, except that an estimate of human exposure (E_{ijkm}) has replaced the dose (d), which is usually a known quantity administered to a bioassay animal. All E_{ijkm} are calculated as discussed above (see **Exposure Dose Determination** in **Exposure Assessment**). When local consumption rate data are unavailable, a range of E_{ijkm} and corresponding risk estimates may be calculated based on a range of assumed consumption values. Estimates of $q_1{}^*_m$ are available in IRIS. Note that Equation 9 is only valid for estimated risks below 10^{-2}.

Estimation of upper-limit risk associated with the average mixed-species diet follows a similar approach, except that the average effective dose (E_{jkm}) of chemical m from a mixed-species diet, calculated from Equation 8 above, replaces the species-specific exposure (E_{ijkm}) in Equation 9. Calculation of the average effective dose was discussed earlier (see **Exposure Assessment, Exposure Dose Determination**).

Noncarcinogenic Effects

Noncarcinogenic risk may be evaluated by calculating the ratio of the estimated chemical intake to the RfD as follows:

$$H_{ijkm} = \frac{E_{ijkm}}{RfD_m} \quad (10)$$

where:

H_{ijkm} = Hazard Index of a health effect from intake of chemical m associated with fishery species i for human subpopulation j in area k (dimensionless)

RfD_m = Reference Dose for chemical m (mg kg^{-1} day^{-1})

and E_{ijkm} is defined as above. RfD_m values are given in IRIS (U.S. EPA 1987a).

When all significant exposure routes and sources are taken into account, the estimated total exposure for all routes replaces E_{ijkm} in the numerator of Equation 10 and the resulting hazard index is compared to a value of 1.0 to evaluate the chemical hazard (Stara et al. 1983; U.S. EPA 1985b). Values of the hazard index for total exposure or of H_{ijkm} that are above 1.0 indicate that the estimated exposure is potentially of concern. Above 1.0, increasing values of either hazard index indicate increasing hazard. However, the hazard index does not define a dose response relationship, and its numerical value should not be regarded as a direct estimate of risk.

Because H_{ijkm} as calculated by Equation 10 do not account for exposures other than that from consumption of single fisheries species, values of H_{ijkm} substantially below 1.0 do not necessarily indicate a lack of significant risk overall. Although species-specific hazard indices are useful for evaluating whether contamination of any single species is of concern, two problems remain:

- How can hazards from mixed-species diets of fish and shellfish be evaluated?
- How should exposures from sources other than consumption of contaminated fish and shellfish (either single-species or mixed-species diets) be taken into account?

To address the first question above, one approach would be to sum H_{ijkm} values across all species to obtain a hazard index, H_{jkm}, associated with the entire fishery. However, H_{jkm} could not be interpreted as representative of actual hazard to individuals, since the sum of estimated exposures across species will not be the same as exposures associated with the mixed-species diets of individuals (see above, **Exposure Assessment, Exposure Dose Determination, Mixed-Species Diet**). An alternative approach recommended here is to use the average effective dose (E_{jkm}) for mixed-species diets to calculate a hazard index. This hazard index for mixed-species diets still does not account for exposures due to other sources.

To address the second question above, the sum of exposures from all sources should be compared to the RfD to evaluate total hazard. Guidance on estimation of exposures due to other sources is available in U.S. EPA (1986b,f). If exposure estimates for sources other than the fishery are not available, then some relatively small fraction of the RfD (e.g., 0.1) could be assigned to intake from consumption of fish and

shellfish. This fractional RfD would then replace the RfD in the denominator of the hazard index. The index would be compared to a value of 1.0 to evaluate the potential for concern. However, the uncertainties associated with such an approach should be clearly stated. Further research on this problem is clearly needed.

The margin of exposure (MOE) is an alternative indicator of noncarcinogenic risk. The MOE is the ratio of the NOAEL to an estimated exposure dose. When the MOE is equal to or greater than the product of the uncertainty factor and the modifying factor used to derive the RfD, the level of regulatory concern is usually low (see U.S. EPA 1987a for details of the derivation of MOE). Concerns about mixed-species diets and exposures from non-fishery sources, as discussed above for hazard indices, also apply to MOE for exposure to contaminated fisheries.

Chemical Mixtures

U.S. EPA (1986d) discussed various models for assessment of the upper limit to risk from chemical mixtures. Because of present data limitations and the complexity of possible contaminant interactions, it is virtually impossible at present to predict synergistic or antagonistic effects of most chemical mixtures. The approach used most frequently for multiple-chemical assessment is the additive-risk (or response-additive) model. Thus, total upper-limit risk for a chemical mixture is usually estimated as the sum of upper-limit risks for carcinogens or of hazard indices for noncarcinogens. A sum of noncarcinogenic hazard indices should be calculated only for a group of chemicals acting on the same target organ (Stara et al.1983). The numerical estimates obtained using the response-additive model are useful in terms of relative comparisons (e.g., among fishing areas or among fishery species). However, risk estimates for chemical mixtures should be regarded only as very rough measures of absolute risk (U.S. EPA 1986d). Because technological limitations preclude analyzing fishery samples for all potentially toxic chemicals, risk estimates for chemical mixtures should not be interpreted as estimates of total chemical risk associated with ingestion.

Presentation and Interpretation of Results

Examples of formats for presenting the results of risk assessments to risk managers or technical audiences are provided below. These formats are adaptable to any level of summary analysis (e.g., subpopulation vs.total exposed population, individual fishery species vs. average across species). Approaches to presentation of supporting documentation on assumptions and uncertainties are also described. Interpretation of the results is largely a function of risk management. As such, guidance on interpretation of risk estimates to support decisionmaking is beyond the scope of this manual. Nevertheless, a brief discussion of risk comparisons (e.g., estimated risks for various fish species; estimated risk vs. acceptable risk defined by policy) is provided to alert the reader to the interface between risk assessment and risk management. Supplementary information, such as comparisons of contaminant concentrations with FDA action levels, is addressed in the final section below.

Presentation Format

The results of risk assessment may be summarized in both tabular and graphic format. All final estimates of risk should be rounded to one significant digit (or an order of magnitude if appropriate). The EPA classification of the qualitative weight of evidence for carcinogenicity should be shown in brackets adjacent to final risk estimates for carcinogens (U.S. EPA 1986a). To guide the reader's interpretation of the information presented, supporting text should describe assumptions, uncertainties, and any caveats about the results. All individual and population-level risk estimates should be interpreted as plausible-upper-limit values for the stated assumptions and exposure conditions.

Summary Tables

An example format for summarizing an exposure analysis is shown in Table 6. The table format allows storage of quantitative information in a computer spreadsheet. Columns of notes containing references to sources of information can easily be added to the spreadsheet to further document the exposure analysis.

TABLE 6.
Example Tabular Format for Display of Quantitative Risk Assessment for Consumption of Fish and Shellfish

	Exposure Determination							Risk Determination				
								Carcinogens			Noncarcinogens	
Substance	Concentration in Medium	Contact Rate (mg/kg)[a]	Total Daily Contact (g/day)[b]	Exposure Duration (mg/day)	Absorption Coefficient (years)	Body Weight (0-1.0)[c]	Exposure Value (kg)	Potency Factor (mg/kg/d)	Upper Limit l/(mg/kg/d)	Weight of Risk	RfD Evidence	Hazard (mg/kg/d)Index
PCBs	0.007	6.5	4.6E-05	70.0	1.0	70	6.5E-07	4.34	3E-06	B2	N/A[d]	N/A
	0.004	6.5	2.6E-05	70.0	1.0	70	3.7E-07	4.34	2E-06	B2	N/A	N/A
	0.010	6.5	6.5E-05	70.0	1.0	70	9.3E-07	4.34	4E-06	B2	N/A	N/A
PCBs	0.007	20.0	1.4E-04	70.0	1.0	70	2.0E-06	4.34	9E-06	B2TN/A	N/A	
	0.004	20.0	8.0E-05	70.0	1.0	70	1.1E-06	4.34	5E-06	B2	N/A	N/A
	0.010	20.0	2.0E-04	70.0	1.0	70	2.9E-06	4.34	1E-05	B2	N/A	N/A
Hg	0.157	6.5	1.0E-03	70.0	1.0	70	1.5E-05	N/A	N/A	[e]	2.9E-04	5E-02
	0.008	6.5	5.2E-05	70.0	1.0	70	7.4E-07	N/A	N/A	[e]	2.9E-04	3E-03
	0.478	6.5	3.1E-03	70.0	1.0	70	4.4E-05	N/A	N/A	[e]	2.9E-04	2E-01
Hg	0.157	20.0	3.1E-03	70.0	1.0	70	4.5E-05	N/A	N/A	[e]	2.9E-04	2E-01
	0.008	20.0	1.6E-04	70.0	1.0	70	2.3E-06	N/A	N/A	[e]	2.9E-04	8E-03
	0.478	20.0	9.6E-03	70.0	1.0	70	1.4E-04	N/A	N/A	[e]	2.9E-04	5E-01

[a] Concentration of contaminant in fisheries species of concern (mg/kg = ppm by mass, wet weight).
[b] Amount of fish/shellfish ingested per day, prior to accounting for absorption efficiency, etc.
[c] Ratio of g of contaminant absorbed per g of contaminant ingested, or correction factor to account for differential absorption by humans and bioassay animals (see text, **Exposure Assessment, Exposure Dose Determination**).
[d] N/A = not applicable.
[e] Carcinogenicity of methyl Hg has not been evaluated by EPA Carcinogen Assessment Group. Hg is typically treated as a noncarcinogen in risk assessment.

It should be emphasized that some variables are capable of being measured relatively precisely (e.g., contaminant concentrations in fish tissue), whereas others may only be estimated on an order-of-magnitude basis (e.g., Carcinogenic Potency Factor). The precision and accuracy of the final risk estimates are directly related to the precision and accuracy of the variables incorporated into the equations used to calculate exposure and risk.

Quantitative uncertainty analyses such as sensitivity analysis are easily performed with a spreadsheet by calculating exposure estimates for low, mid, and high values of key variables within their respective plausible ranges. Specification of probability distributions for key variables is an alternative method of uncertainty analysis requiring graphical models (see below, **Uncertainty Analysis**). In the example shown in Table 6, the average, minimum, and maximum concentrations of each contaminant [PCBs and mercury (Hg)] are used to estimate potential health risk, thereby accounting for uncertainty in chemical analyses. Also, risks are estimated for two consumption rate estimates (6.5g/day and 20 g/day). Note that spreadsheet summaries of quantitative information should be supported by a text discussion of qualitative uncertainties such as the weight of evidence for the health effect of concern.

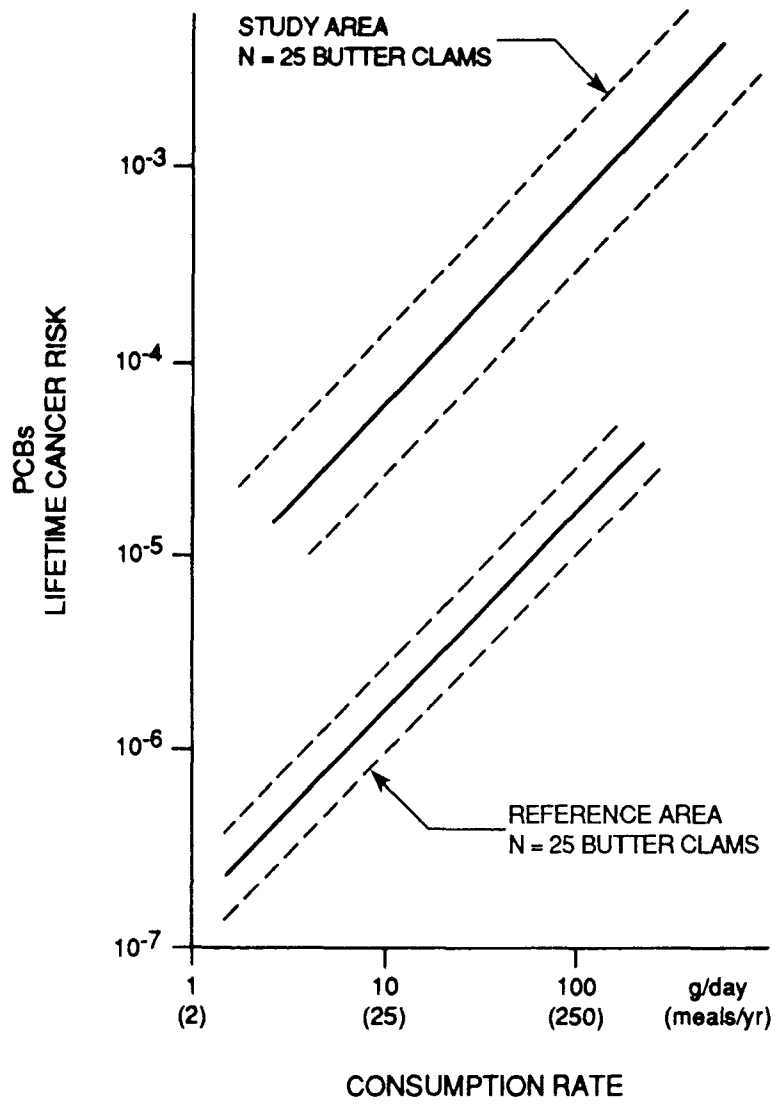
Summary Graphics

Presentation of risk assessment results in graphic form may include:

- Plots of estimated risk vs. consumption rate
- Plots of estimated risk vs. contaminant concentration in edible tissue of fish or shellfish
- Summary maps of risk estimates for different geographic locations or individual sampling stations
- Histograms of estimated risk by fishery species, human subpopulation, or geographic location.

Because estimated risk for a given area and fishery species varies with consumption rate and because consumption rates vary greatly among individual humans, the first approach above is recommended as a primary means of presenting risk assessment results. Actual consumption patterns of the exposed population may or may not be estimated (see above, **Exposure Assessment**). If they are, estimates of average consumption rate (and 95 percent confidence limits) can be identified in a footnote (e.g., Figure 7). Uncertainty in chemical measurements can be illustrated by plotting lines corresponding to the minimum and maximum (or 95 percent confidence limit) values of contaminant concentrations in fishery species, as well as the mean concentration (e.g., each solid line in Figure 7). As an interpretive aid, risk assessment results for a reference area can be presented along with those for the study area.

Other approaches noted above can be used to supplement plots of risk vs. consumption. Summary maps and histograms may be especially useful for presentation of detailed results of spatial analyses by human subpopulation or by fishery species. Plots of risk vs. contaminant



PCBs Weight-of-evidence classification:
PROBABLE HUMAN CARCINOGEN [B2]

All cancer risks are plausible-upper-limit estimates of excess risk based on linearized multistage procedure and assumptions summarized in the text. Solid lines are risks associated with average PCB concentrations in butter clams. Dashed lines are for uncertainty range (e.g., 95 percent confidence limits) for average concentrations of PCBs, not the total uncertainty. Actual risks are likely to be lower than those shown above and may be zero.

Figure 7 Example graphic format for display of quantitative risk assessment results for hypothetical study area and reference area.

concentration for selected consumption rates and species (e.g., Figure 8) aid in rapid interpretation of tissue contamination data.

Risk Comparisons

Interpretation of carcinogenic risk assessment results may be based on comparison of estimated health risks for the study area with:

- Estimated health risks for consumption of fishery species from a reference area
- Estimated health risks for consumption of alternative foods (e.g., charcoal-broiled steak, marketplace foods).

An example of comparison with reference-area risk estimates is shown in Figure 7 above. Comparative risks for alternative foods can be summarized in a table or histogram. Wilson and Crouch (1987) point out the importance of comparing the results of risk assessments with similar assessments of common activities to provide perspective for interpretation of the results by risk managers and the general public. Risk comparisons should be based on consistent exposure analysis and risk extrapolation models. Analogous exposure scenarios should be used for each risk estimate being compared (i.e., either worst case, plausible-upper limit, average, or lower limit). A single model should be applied consistently to calculate exposure and risk. A linear extrapolation model, such as Equations 2 and 6 above, is justified in general if the excess risk attributed to the contaminant of concern is regarded as a marginal risk, added to a background of relatively high cancer incidence from all other causes not being modeled (Crump et al. 1976; Omenn 1985).

When interpreting the results of risk assessments, risk managers may define an acceptable level of risk to provide a criterion for judging the significance of potential health effects. The term "acceptable risk" is used to denote the maximum risk considered tolerable by an individual or a regulatory agency. An acceptable risk level has not been strictly determined by EPA. Although acceptable risk levels must be defined on a case-specific basis, some perspective can be gained by examining previous risk management decisions. For example, past regulatory decisions by U.S. federal agencies have allowed environmental risks as high as 10^{-3} to 10^{-2} when the exposed population was relatively small (Travis et al. 1987). For exposures of the entire U.S. population, the acceptable risk level has usually been defined as 10^{-6}.

Summary of Assumptions

Assumptions underlying the risk assessment model and estimates of model variables should be summarized in a concise format (see Table 7 for summary of some assumptions and numerical estimates used in the approach presented in this manual). Specific assumptions adopted on a case-by-case basis should be summarized in a similar fashion.

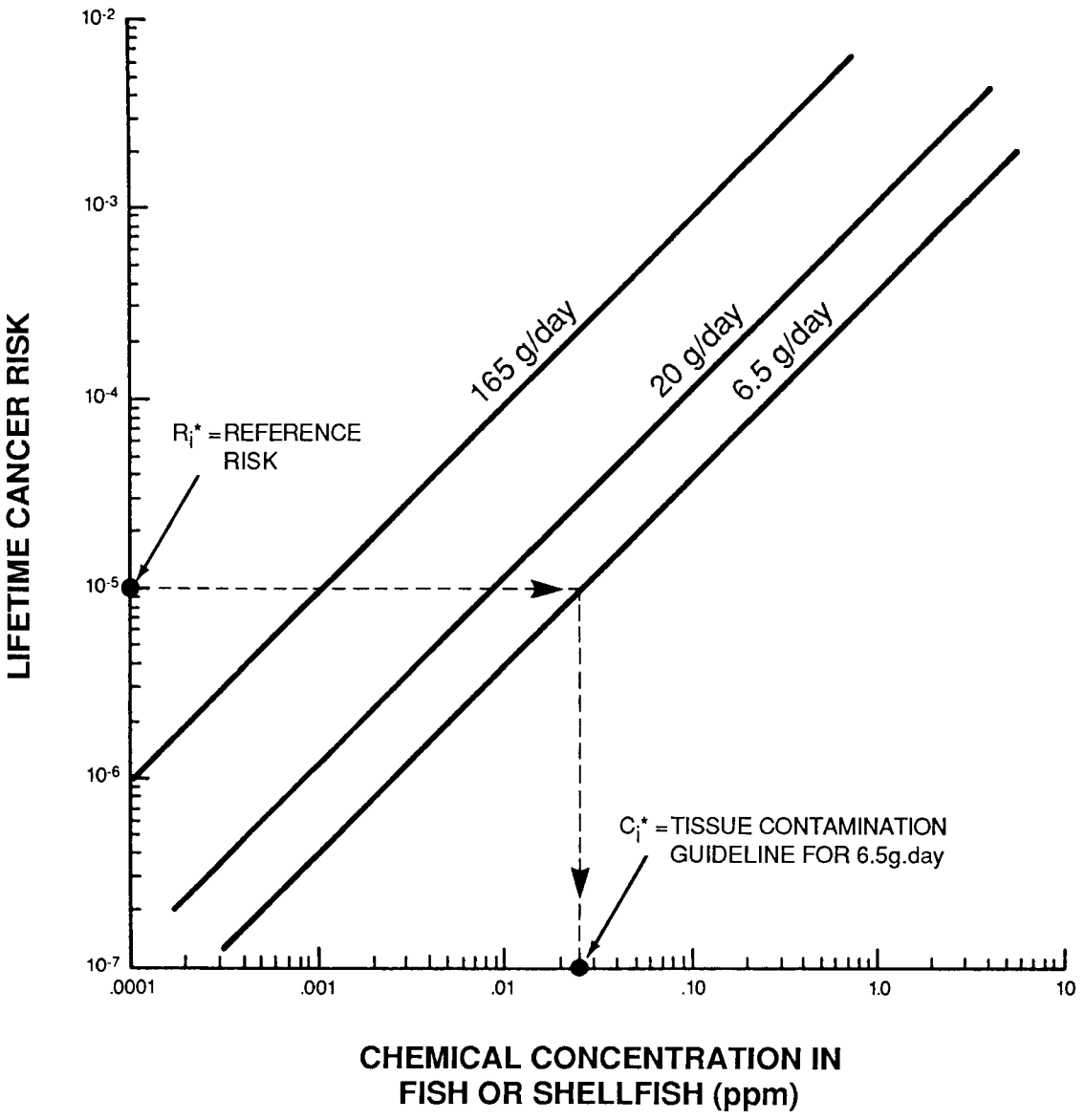


Figure 8 Plausible-upper-limit estimate of lifetime excess cancer risk vs. concentration of a chemical contaminant in fish or shellfish (ppm wet wt.) at selected ingestion rates.

TABLE 7. Summary of Assumptions and Numerical Estimates Used in Risk Assessment Approach

Reference	Assumption/Estimates	Parameter
		Exposure Assessment:
Worst case for parent compounds. Net effect on risk is uncertain.	No effect on cooking.	Contaminant concentrations in tissues of indicator species
Low, moderate, and high values for U.S. population (see text).	6.5 g/day, 20 g/day, 165 g/day	Average consumption rate[a]
U.S. EPA 1980b; 1986a,b	1.0, Assumes efficiency of absorption of contaminants is same for humans and bioassay animals.	Gastrointestinal absorption coefficient
U.S. EPA 1980b; 1986a,b	70 years	Exposure duration
U.S. EPA 1986a,b	70 kg (= average adult male)	Human body weight
		Risk Characterization:
U.S. EPA 1980b, 1986a, 1987a	Linearized Multistage, At risks less than 10^{-2}: Risk = Exposure x Potency	Carcinogenic risk model
U.S. EPA 1987a	Potency factors are based on low-dose extrapolation from animal bioassay data. Upper bound of 95 percent confidence interval on potency is used.	Carcinogenic potency
U.S. EPA 1987a	RfDs for noncarcinogens compared with estimated exposure.	Noncarcinogenic risk

[a] Estimates of consumption for local population should be used in place of values shown for U.S. population whenever possible.

Other assumptions, such as general approaches or assumptions underlying models that are commonly used to estimate risk, can be summarized in the text of a risk assessment document. Some additional assumptions involved in applying the risk assessment approach described in this manual include the following:

- Adverse effects in experimental animals are indicative of adverse effects in humans (e.g., lifetime incidence of cancer in humans is the same as that in animals receiving an equivalent dose in units of mg per surface area)
- Dose-response models can be extrapolated beyond the range of experimental observations to yield plausible-upper-bound estimates of risk at low doses
- A threshold dose does not exist for carcinogenesis
- A threshold dose (e.g., NOAEL) exists for noncarcinogenic effects
- The most sensitive animal species is appropriate to represent the response of humans
- Cumulative incidence of cancer increases in proportion to the third power of age (this assumption is used to estimate lifetime

incidence when data are available only from less-than-lifetime experiments)

- For carcinogens, average doses are an appropriate measure of exposure dose, even if dose rates vary over time
- In the absence of pharmacokinetic data, the effective (or target organ) dose is assumed to be proportional to the administered dose
- Risks from multiple exposures in time are additive
- For each chemical, the absorption efficiency of humans is equal to that of the experimental animal
- If available, human data are preferable to animal data for risk estimation
- For chemical mixtures, risks for individual chemicals are additive. However, the total sum of individual chemical risks is not necessarily the total risk associated with ingestion of contaminated fish or shellfish because some important toxic compounds may not have been identified and quantified.

Uncertainty Analysis

Uncertainty analysis is an integral part of risk assessment. The EPA guidelines on exposure assessment describe general approaches for characterizing uncertainty (U.S. EPA 1986b). Methods for uncertainty analysis are discussed by Cox and Baybutt (1981), Morgan (1984), and Whitmore (1985). A detailed discussion of procedures is beyond the scope of the present effort. General approaches to uncertainty analysis will be described briefly after a discussion of sources of uncertainty.

Sources of Uncertainty

Uncertainties in the risk assessment approach presented in this manual arise from the following factors:

1. Uncertainties in the determination of the weight-of-evidence classification for potential carcinogens.
2. Uncertainties in estimating Carcinogenic Potency Factors or RfDs, resulting from:

- Uncertainties in extrapolating toxicologic data obtained from laboratory animals to humans
- Limitations in quality of animal study
- Uncertainties in high- to low-dose extrapolation of bioassay test results, which arise from practical limitations of laboratory experiments and variations in extrapolation models

3. Variance of sitespecific consumption rates and contaminant concentrations
4. Uncertainties in the selection of 6.5 g/day, 20 g/day, and 165 g/day as assumed consumption rates when site-specific data are not available
5. Uncertainties in the efficiency of assimilation (or absorption) of contaminants by the human gastrointestinal system (assumed

to be the same as assimilation efficiency of the experimental animal in the bioassay used to determine a Carcinogenic Potency Factor or RfD)

6. Variation of exposure factors among individuals, such as:
    - Variation in fishery species composition of the diet among individuals
    - Variation in food preparation methods and associated changes in chemical composition and concentrations due to cooking.

Variance in estimates of carcinogenic potency or RfDs (#1 above) account for one major uncertainty component in most risk assessments. Chemical potencies are estimated only on an order-of-magnitude basis, whereas analytical chemistry of tissues is relatively precise (on the order of $\pm$20 percent). The choice of a low-dose extrapolation model greatly influences estimates of the Carcinogenic Potency Factor and calculated risks. This uncertainty contributed by the model is substantial when predicting risks below 10^{-2}. For example, the plausible-upper limit to lifetime cancer risk associated with 50 μg/L tetrachloroethene in drinking water ranges from about 10^{-6} for the probit model to 10^{-2} for the Weibull model (Cothern et al. 1986). Model uncertainty is important when considering absolute risk estimates (e.g., Cothern et al. 1986), but less important for relative risk comparisons.

Uncertainty analysis conducted by previous researchers illustrates the variability of risk estimates and potency factors for a given extrapolation model. For example, the coefficient of variation for the mean value of potency generally ranged from 2 to 105 percent for each drinking water contaminant studied by Crouch et al. (1983). This uncertainty arose mainly from error associated with experimental bioassay data for a single animal species. Among bioassay species, the potency of a given chemical may vary only slightly or up to approximately 1,000-fold, depending on the chemical in question (Clayson et al. 1983). Thus, the uncertainty associated with extrapolating potency factors from laboratory animals to humans may be much greater than the uncertainty associated with animal bioassay techniques. By comparison, the range of potencies among carcinogens covers 7-9 orders of magnitude (Clayson et al. 1983; U.S. EPA 1985a). Relative risk comparisons among chemicals can be made more confidently when the range of potency factors is broad. Note that such comparisons should also include consideration of the qualitative uncertainty (e.g., weight of evidence) in assessing the specific health effects of chemicals, including mode of action, latency period, and target organs.

In conclusion, uncertainty ranges (e.g., 95 percent confidence intervals) around estimates of mean risk may typically span at least several orders of magnitude. The approach taken by U.S. EPA (1980b, 1985a, 1986a) and followed herein is to estimate a plausible-upper limit to risk. In this way, it is unlikely that risk will be underestimated substantially. Moreover, the plausible-upper-limit estimate serves as a consistent basis for relative risk comparisons. However, the effects of compounding conservative assumptions should be evaluated to provide perspective on risk assessment results.

Approaches to Uncertainty Analysis

Analysis of uncertainty in a risk assessment should address both quantitative and qualitative uncertainty. Quantitative uncertainty analysis deals primarily with variation in numerical estimates of exposure and risk that results from changing the values of variables in mathematical models used to calculate the estimates (e.g., low-dose extrapolation models). Characterization of variability in chemical measurements, food consumption rates, and Carcinogenic Potency Factors (or RfDs) and its effect on estimates of exposure and risk is an example of quantitative uncertainty analysis. A qualitative uncertainty analysis includes primarily a summary of limitations of the data and the weight of evidence for toxic effects of concern. A discussion of qualitative uncertainties should present information from IRIS on the level of confidence that EPA places in each Carcinogenic Potency Factor and RfD.

General approaches to treatment of uncertainty in variables used in risk analysis models include the following (Morgan 1984):

- Perform analysis using **single-value-best-estimates** for model variables **without uncertainty analysis**
- Perform **single-value-best-estimate** analysis, **with sensitivity calculations** and appropriate discussion of uncertainty
- Estimate some **measure of uncertainty** (e.g., standard deviation) for each model variable and use **error propagation** methods to estimate uncertainty of final exposure or risk value
- Characterize subjectively the **probability distribution** of each model variable and **propagate error** through stochastic simulation
- Characterize important model variables using a **parametric model** and perform risk analysis using various **plausible values** of each of the variables
- Determine upper and lower **bounds** on model variables to yield **order-of-magnitude estimates** and range of possible answers.

Morgan (1984) refers to the first two approaches as "single-value-best-estimate analysis," to the second two as "probabilistic analysis," and to the final two as "parametric/bounding analysis." The analytical strategies listed above are in roughly descending order, based on the amount of uncertainty in the model variables. Single-value-best-estimate analysis is appropriate when model variables are precisely known. Bounding analysis is most appropriate when values of model variables are not well-known. The techniques listed above do not address model uncertainty, which must be handled by exploratory examination of outcomes based on alternative model equations.

The choice of a method for uncertainty analysis will depend on the amount and quality of exposure data and on the study objectives. Quantitative uncertainty analysis is applied mainly to exposure variables, such as contaminant concentration in fishery species and consumption rate. Following U.S. EPA (1980b, 1984a, 1985a), an

upper-bound estimate of the Carcinogenic Potency Factor is used in carcinogenic risk calculations. Substitution of the mean estimate or the lower bound of the 95 percent confidence interval for the potency factor in the risk calculations is generally not done because of the instability of these estimates (U.S. EPA 1980b, 1986a).

The U.S. EPA (1986b) guidelines on exposure assessment and Whitmore (1985) summarize the primary methods for characterizing uncertainty in exposure estimates in relation to attributes of the exposed population and the exposure data. In many cases, data will be sufficient only to use parametric/bounding analysis, as described above. In any case, a discussion of qualitative uncertainties in the analysis should always accompany presentation of risk assessment results. For example, limitations of data related to inadequate survey design or insensitive analytical chemistry methods should be described. The extent of chemical data for geographic locations of interest should be summarized. Insufficient information on characteristics of the exposed population should be noted. The level of confidence in data used to develop RfDs, Carcinogenic Potency Factors, and weight-of-evidence classifications based on IRIS Chemical Files should be indicated.

Supplementary Information

Additional information to support risk assessment of contaminated fish and shellfish consumption may include:

- Comparisons of tissue concentrations of contaminants with FDA action (or tolerance) levels
- Statistical comparisons of mean contaminant concentrations among fishery species and among locations
- Statistical comparisons of mean contaminant concentrations in fishery species with those in other foods.

FDA limits on contaminants in fishery products are shown in **Appendix I.** Limitations to use of these values for assessing health risk were discussed earlier (see above, **Overview of Risk Assessment**). For comparison, legal limits on fishery contaminants established by other countries are also provided in **Appendix I.**

Some resource management agencies have developed advisories based simply on comparisons between contaminant concentrations in fishery species and those in corresponding species from reference or control areas. For example, the Northeast Shellfish Sanitation Commission has established "alert levels" for metals in shellfish as the concentration equal to one standard deviation above the mean background (reference) concentration. These alert levels are not based on health effects, but assume that the level of concern is related to an elevation above average background conditions.

REFERENCES

Ames, B.N., R. Magaw, and L.S. Gold. 1987. "Ranking possible carcinogenic hazards." Science 236:271-280.

Anderson, E., N. Browne, S. Duletsky, J. Ramig, and T. Warn. 1985. "Development of statistical distributions or ranges of standard factors used in exposure assessments." OHEA-E-161. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Washington, DC. 47 pp. + appendices.

Armstrong, R.W., and R.J. Sloan. 1980. "Trends in levels of several known chemical contaminants in fish from New York State waters." Tech. Report No. 80-2. New York State Department of Environmental Conservation, Albany, NY. 77 pp.

Bellin, J.S., and D.G. Barnes. 1986. "Interim procedures for estimating risks associated with exposures to mixtures of chlorinated dibenzo-p-dioxins and dibenzofurans (CDDs and CDFs)." Risk Assessment Forum. U.S. Environmental Protection Agency, Washington, DC. 27 pp. + appendices.

Belton, T., R. Roundy, and N. Weinstein. 1986. "Urban fisherman: managing the risks of toxic exposures." Environment 28:18-37.

Boehm, P.D. 1984. "The Status and Trends Program: recommendations for design and implementation of the chemical measurement segment." Workshop Report. Prepared for National Oceanic and Atmospheric Administration, Rockville, MD. Prepared by Battelle, Duxbury, MA.

Briggs, G.G. 1981. "Theoretical and experimental relationships between soil adsorption, octanol-water partition coefficients, water solubilities, bioconcentration factors, and the parachor." J. Agric. Food Chem. 29:1050-1059.

Brown, D., A. Friedman, and W. MacLeod, Jr. 1985a. "Quality assurance guidelines for chemical analysis of aquatic environmental

samples." Draft Report. Prepared by National Analytical Facility Region X and National Oceanographic and Atmospheric Administration, for Seattle District, U.S. Army Corps of Engineers, Seattle, WA.

Brown, M.P., M.B. Werner, R.J. Sloan, and K.W. Simpson. 1985b. "Polychlorinated biphenyls in the Hudson River." Environ. Sci. Technol. 19:656-661.

Brumelle, S., P. Nemetz, and D. Casey. 1984. "Estimating means and variances: the comparative efficiency of composite and grab samples." Environ. Monit. and Assess. 4:81-84.

Burns, L.A., D.M. Cline, and R.R. Lassiter. 1981. "Exposure analysis and modeling system (EXAMS): user manual and system documentation." U.S. Environmental Protection Agency, Environmental Research Laboratory, Athens, GA.

Callahan, M.A., M.W. Slimak, N.W. Gable, I.P. May, C.F. Fowler, J.R. Freed, P. Jennings, R.L. Durfee, F.C. Whitmore, B. Amestri, W.R. Mabey, B.R. Holt, and C. Gould. 1979. "Water-related environmental fate of 129 priority pollutants." Volumes I and II. EPA-440/4-79-029a/b. U.S. Environmental Protection Agency, Washington, DC. Available from NTIS as PB80-204373 (Volume 1) and PB80-204381 (Volume II).

Capuzzo, J.M., A. McElroy, and G. Wallace. 1987. "Fish and shellfish contamination in New England waters: an evaluation and review of available data on the distribution of chemical contaminants." Coast Alliance, Washington, DC. 59 pp. + appendices.

Chiou, C.T., D.W. Schmedding, J.H. Block. 1981. "Correlation of water solubility with octanol-water partition coefficient." J. Pharmaceutical Sciences 70:1176-1177.

Clarkson, et al. 1973. As cited in IRIS.

Clayson, D.B., D. Krewski, and I.C. Munro. 1983. "The power and interpretation of the carcinogenicity assay." Regul. Toxicol. and Pharmacol. 3:329-348.

Cohen, J. 1977. Statistical power analysis for the behavioral sciences. Academic Press, New York, NY.

Connor, M.S. 1984a. "Comparison of the carcinogenic risks from fish vs. groundwater contamination by organic compounds." Environ. Sci.Technol. 18:628-631.

Connor, M.S. 1984b. "Fish/sediment concentration ratios for organic compounds." Environ. Sci. Technol. 18:31-35.

Cordle, F., P. Corneliussen, C. Jelinek, B. Hackley, R. Lehman, J. McLaughlin, R. Rhoden, and R. Shapiro. 1978. "Human exposure to polychlorinated biphenyls and polybrominated biphenyls." Environ. Health Perspectives 24:157-172.

Cothern, C.R., W.A. Coniglio, and W.L. Marcus. 1986. "Estimating risk to human health." Environ. Sci. Technol. 20:111-116.

Cox, D.C., and P. Baybutt. 1981. "Methods of uncertainty analysis: a comparative survey." Risk Analysis 1:251-258.

Crouch, E.A.C., R. Wilson, and L. Zeise. 1983. "The risks of drinking water." Water Resour. Res. 19:1359-1375.

Crump, K.S., D.G. Hoel, C.H. Langley, and R. Peto. 1976. "Fundamental carcinogenic processes and their implications for low dose risk assessment." Cancer Res. 36:2973-2979.

Dedrick, R.L. 1973. "Animal scale up." J. Pharmacokinet. Biopharm. 1:435-461.

DeVault, D.S., W.A. Willford, R.J. Hesselberg, D.A. Nortrupt, E.G.S. Rundberg, A.K. Alwan, and C. Bautista. 1986. "Contaminant trends in lake trout (Salvelinus namaycush) from the upper Great Lakes." Arch. Environ. Contam. Toxicol. 15:349-356.

Dourson, M.L., and J.F. Stara. 1983. "Regulatory history and experimental support of uncertainty (safety) factors." Regul. Toxicol. and Pharmacol. 3:224-238.

Farrington, J.W., E.D. Goldberg, R.W. Risebrough, J.H. Martin, and V.T. Bowen. 1983. U.S. "Mussel Watch 1976-1978: An overview of the trace-metal, DDE, PCB, hydrocarbon, and artificial radionuclide data." Environ. Sci. Technol. 17:490-496.

Finch, R. 1973. "Effects of regulatory guidelines on the intake of mercury from fish - the MECCA project." Fish. Bull. 71:615-626.

Flamm, W.G., and J.S. Winbush. 1984. "Role of mathematical models in assessment of risks and in attempts to define management strategy." Fundam. Appl. Toxicol. 4:395-401.

Food Safety Council. 1980. Proposed system for food safety assessment. Food Safety Council, Washington, DC. 160 pp.

Food Safety Council. 1982. A proposed food safety evaluation process. Food Safety Council, Washington, DC. 142 pp.

Freireich, E.J., E.A. Gehan, D.P. Rall, L.H. Schmidt, and H.E. Skipper. 1966. "Quantitative comparison of toxicity of anticancer agents in mouse, rat, hamster, dog, monkey, and man." Cancer Chemother. Rep. 50:219-244.

Gahler, A.R., R.L. Arp, and J.M. Cummins. 1982. "Chemical contaminants in edible non-salmonid fish and crabs from Commencement Bay, Washington." U.S. Environmental Protection Agency, Environmental Services Division, Seattle, WA. 117 pp.

Games, L.M. 1983. "Practical applications and comparisons of environmental exposure assessment models." pp. 282-299. In: Aquatic Toxicology and Hazard Assessment: Sixth Symposium, ASTM STP 802. W.E.

Bishop, R.D. Cardwell, and B.B. Heidolph (eds). American Society for Testing and Materials, Philadelphia, PA.

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, and E.L. Gunderson. 1986a. "Pesticides, selected elements, and other chemicals in adult total diet samples, October 1980 - March 1982." J. Assoc. Off. Anal. Chem. 69:146-161.

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, and E.L. Gunderson. 1986b. "Pesticides, selected elements, and other chemicals in infant and toddler total diet samples, October 1980 - March 1982." J. Assoc. Off. Anal. Chem. 69:123-145.

Gilbert, R.O. 1987. Statistical methods for environmental pollution monitoring. Van Nostrand Reinhold Company, New York, NY. 320 pp.

Goldberg, E.D., V.T. Bowen, G.H. Farrington, J.H. Martin, P.L. Parker, R.W. Risebrough, W. Robertson, E. Schneider, and Gamble. 1978. "The mussel watch." Environ. Conserv. 5:101-125.

Goldberg, E.D., M. Koide, V. Hodge, R. Flegal, and J. Martin. 1983. "U.S. mussel watch: 1977-1978 results on trace metals and radionuclides." Estuar. Coast. Shelf Sci. 16:69-93.

Gordon, M., G.A. Knauer, and J.H. Martin. 1980. "Mytilus californianus as a bioindicator of trace metal pollution: variability and statistical considerations." Mar. Pollut. Bull. 11:195-198.

Gossett, R.W., D.A. Brown, and D.R. Young. 1983. "Predicting the bioaccumulation of organic compounds in marine organisms using octanol-water partition coefficients." Mar. Poll. Bull. 14:387-392.

Grasso, P., and C. O'Hare. 1976. "Carcinogens in foods." pp. 701-728. In: Chemical Carcinogens. L.E. Searle (ed). ACS Monograph 173. American Chemical Society, Washington, DC.

Green, R.H. 1979. Sampling design and statistical methods for environmental biologists. John Wiley and Sons, Inc., New York, NY. 257 pp.

Hogan, M.D., and D.G. Hoel. 1982. "Extrapolation to man." pp.711-731. In: Principles and Methods of Toxicology. A.W.Hayes (ed). Raven Press, New York, NY.

Horwitz, W., L. Kamps, and K. Boyer. 1980. "Quality assurance in the analysis of foods for trace contaminations." Anal. Chem. 63:1344-1354.

Humphrey, H.E.B. 1983. "Population studies of PCBs in Michigan residents." pp. 299-310. In: PCBs: Human and Environmental Hazards. Chapter 21. F.M. D'Itri and M.A. Kamrin (eds). Butterworth Publishing, Boston, MA.

Humphrey, H.E.B. 1987. "The human population: an ultimate receptor for aquatic contaminants." Hydrobiol. 149:75-80.

Humphrey, H.E.B. 1988. "Chemical contaminants in the Great Lakes: the human health aspect." pp. 153-165. In: Toxic Contaminants and Ecosystem Health: A Great Lakes Focus. M.J. Evans (ed). John Wiley & Sons, New York, NY.

International Agency for Research on Cancer. 1978. "Working group on the evaluation of the carcinogenic risk of chemicals to humans." In: International Agency for Research on Cancer Monographs. Vol. 18, Polychlorinated Biphenyls. Lyon, France.

Jensen, A.L., S.A. Spigarelli, and M.M. Thommes. 1982. "PCB uptake by five species of fish in Lake Michigan, Green Bay of Lake Michigan, and Cayuga Lake, New York." Can. J. Fish. Aquat. Sci. 39:700-709.

Johnson, M.G. 1987. "Trace element loading to sediments of fourteen Ontario lakes and correlations with concentrations in fish." Can. J. Fish. Aquat. Sci. 44:3-13.

Karickhoff, S.W. 1981. "Semi-empirical estimation of sorption of hydrophobic pollutants on natural sediments and soils." Chemosphere 10:833-846.

Kenaga, E.E., and C.A.I. Goring. 1980. "Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota." pp. 78-115. In: Aquatic Toxicology, Third Symposium. ASTM-STP 707. J.G. Eaton, P.R. Parrish, and A.C. Hendricks (eds). American Society for Testing and Materials, Philadelphia, PA.

Kneip, T.J. 1983. "Public health risks of toxic substances." pp. 577-610. In: Ocean Disposal of Municipal Wastewater: Impacts on the Coastal Environment. Vol. 2. E.P. Myers and E.T. Harding (eds). MITSG 83-33. Massachusetts Institute of Technology, Cambridge, MA.

Ladd, J.M., S.P. Hayes, M. Martin, M.D. Stephenson, S.L. Coale, J. Linfield, and M. Brown. 1984. "California state mussel watch: 1981-1983. Trace metals and synthetic organic compounds in mussels from California's coast, bays, and estuaries. Biennial Report." Water Quality Monitoring Report No. 83-6TS. Sacramento, CA. 81 pp.

Landolt, M.L., F.R. Hafer, A. Nevissi, G. van Belle, K. Van Ness, and C. Rockwell. 1985. "Potential toxicant exposure among consumers of recreationally caught fish from urban embayments of Puget Sound." NOAA Technical Memorandum NOS-OMA-23. National Oceanographic and Atmospheric Administration, Rockville, MD. 104 pp.

Landolt, M., D. Kalman, A. Nevissi, G. van Belle, K. Van Ness, and F. Hafer. 1987. "Potential toxicant exposure among consumers of recreationally caught fish from urban embayments of Puget Sound: final report." NOAA Tech. Mem. NOS OMA 33. National Oceanic and Atmospheric Administration, Rockville, MD. 111 pp.

Lave, L.B. 1987. "Health and safety risk analysis: information for better decisions." Science 236:291-295.

Lave, L.B., and J. Menkes. 1985. "Managing risk: a joint U.S.-German perspective." Risk Analysis 5:17-23.

Leo, A. 20 November 1984. Personal Communication.

Life Systems, Inc. 1985. The endangerment assessment handbook. Draft Report. Prepared for Planning Research Corporation, Chicago, IL, for Office of Waste Programs Enforcement, U.S. Environmental Protection Agency, Washington,DC.

Lindsay, D.G. 1986. "Estimation of the dietary intake of chemicals in food." Food Addit. Contam. 3:71-88.

Lo, M-T., and E. Sandi. 1978. "Polycyclic aromatic hydrocarbons (polynuclears) in foods." Residue Rev. 69:35-86.

Lowrance, W.W. 1976. Of acceptable risk: science and the determination of safety. Willia, Kaufman, Los Altos, CA.

Lyman, W.J., W.F. Reehl, and D.H. Rosenblatt. 1982. Handbook of chemical property estimation methods. McGraw-Hill Book Co., New York, NY.

MacLeod Jr., W., D. Brown, A. Friedman, O. Maynes, and R. Pierce. 1984. "Standard analytical procedures of the NOAA National Analytical Facility, 1984-85, extractable toxic organic compounds." Prepared for the NOAA National Status and Trends Program. NOAA Technical Memorandum NMFS F/NWC-64.

Malins, D.C., B.B. McCain, D.W. Brown, S-L Chan, M.S. Myers, J.T. Landahl, P.G. Prohaska, A.J. Friedman, L.D. Rhodes, D.G. Burrows, W.D. Gronlund, and H.O. Hodgins. 1984. "Chemical pollutants in sediments and diseases of bottom-dwelling fish in Puget Sound, Washington." Environ. Sci. Tech. 18:705-713.

Mantel, N., and M.A. Schneiderman. 1975. "Estimating "safe levels": a hazardous undertaking." Cancer Res. 35:1379.

Matta, M.B., A.J. Mearns, and M.F. Buchman. 1986. Trends in DDT and PCBs in U.S. west coast fish and invertebrates. The National Status and Trends Program for Marine Environmental Quality. Ocean Assessments Division, National Oceanic and Atmospheric Administration, Seattle, WA. 95 pp.

McCallum, M. 1985. Recreational and subsistence catch and consumption of seafood from three urban industrial bays of Puget Sound: Port Gardner, Elliott Bay, and Sinclair Inlet. Washington Department of Social and Health Services, Olympia, WA. 59pp.

McDuffie, B. 1981. "Estimation of octanol/water partition coefficients for organic pollutants using reverse-phase HPLC." Chemosphere 10:73-83.

Means, J.C., S.G. Wood, J.J. Hassett, and W.L. Banwart. 1980. "Sorption of PAH by sediments and soils." Environ. Sci. Technol. 14:1524-1528.

Miller, M.M., S. Ghodbane, S.P. Wasik, Y.B. Tewari, and D.E. Martire. 1984. "Aqueous solubilities, octanol/water partition coefficients, and entropies of melting of chlorinated benzenes and biphenyls." J. Chem. Eng. Data 29:184-190.

Miller, M.M., S.P. Wasik, G.-L. Huang, W.-Y. Shiu, and D. Mackay. 1985. "Relationships between octanol-water partition coefficient and aqueous solubility." Environ. Sci. Technol. 19:522-529.

Mills, W.B., J.D. Dean, D.B. Porcella, S.A. Gherini, R.J.M. Hudson, W.E. Frick, G.L. Rupp, and G.L. Bowie. 1983. Water quality assessment: a screening procedure for toxic and conventional pollutants in surface waters. Vol. 1. Final Report. Prepared for U.S. Environmental Protection Agency, Athens, GA. Tetra Tech, Inc., Lafayette, CA.

Montgomery, R.H., and K.H. Reckhow. 1984. "Techniques for detecting trends in lake water quality." Water Resour. Bull. 20:43-52.

Morgan, M.G. 1984. "Uncertainty and quantitative assessment in risk management." pp.113-130. In: Assessment and Management of Chemical Risks. J.V. Rodricks and R.G. Tardiff (eds). ACS Symposium Ser. 239. American Chemical Society, Washington, DC.

Nash, D.A. 1971. "A survey of fish purchases by socio-economic characteristics." Data Report No.62. National Marine Fisheries Service, Seattle, WA.

National Marine Fisheries Service. 1976. Seafood consumption study, 1973-1974. National Marine Fisheries Service, Washington, DC. p.146.

National Marine Fisheries Service. 1984. "Fisheries of the United States, 1983." Current fishery statistics No. 8320. National Marine Fisheries Service, Washington, DC. 121 pp.

National Marine Fisheries Service. 1986. "Marine recreational fishery statistics survey, Pacific Coast, 1985." Current Fishery Statistics No. 8328, National Marine Fisheries Service, Washington, DC.

National Oceanic and Atmospheric Administration, U.S. Food and Drug Administration, and U.S. Environmental Protection Agency. 1986. Report on 1984-86 Federal survey of PCBs in Atlantic coast bluefish. Data Report. 184 pp. Available from NTIS as PB86-218070/XAB.

National Oceanic and Atmospheric Administration, U.S. Food and Drug Administration, and U.S. Environmental Protection Agency. 1987. Report on 1984-86 Federal survey of PCBs in Atlantic coast bluefish. Interpretive Report. 169 pp. Available from NTIS as PB87-214672/XAB.

National Research Council. 1983. Risk assessment in the federal government: managing the process. The Committee on the Institution of Means for the Assessment of Crisis to Public Health. Washington, DC.

National Toxicology Program. 1982. Third annual report on carcinogens. NTP 82-330. U.S. Department of Health and Human Services, Public Health Service, Washington, DC. 327 pp. + 5 appendices.

National Toxicology Program. 1985. Fourth annual report on carcinogens. NTP 85-002. U.S.Department of Health and Human Services, Public Health Service, Washington, DC. 333 pp.

Nauen, C.E. 1983. "Compilation of legal limits for hazardous substances in fish and fishery products." FAO Fisheries Circular No.764. Food and Agriculture Organization of the United Nations, Rome, Italy. 102 pp.

Omenn, G. 1985. "A framework for risk assessment." In: Risk Assessment in Occupational and Environmental Health. (Short course text). University of Washington, Northwest Center for Occupational Health and Safety, Seattle, WA.

Onishi, Y. 1985a. "Chemical transport and fate in risk assessment." pp. 117-154. In: Principles of Health Risk Assessment. P.F. Ricci (ed). Prentice-Hall, Inc., Englewood Cliffs, NJ.

Onishi, Y. 1985b. "Chemical transport and fate models." pp. 155-234. In: Principles of Health Risk Assessment. P.F. Ricci (ed). Prentice-Hall, Inc., Englewood Cliffs, NJ.

Ozretich, R.J., and W.P. Schroeder. 1985. Determination of priority pollutant organic pollutants in marine sediment, tissue, and reference materials utilizing bonded-phase sorbants. U.S. Environmental Protection Agency, Environmental Research Laboratories, Narragansett, RI, and Newport, OR.

Pao, E.M., K.H. Fleming, P.M. Guenther, and F.J. Nickle. 1982. "Foods commonly eaten by individuals: amount per day and per eating occasion." Home Economics Records Report No. 44. U.S. Department of Agriculture, Washington, DC.

Pastorok, R.A. 1986. "Damage assessment model for fisheries contaminated by toxic chemicals." Paper presented at sixth International Ocean Disposal Symposium, Asilomar Conference Center, Pacific Grove, CA. 34 pp.

Peddicord, R.K. 1984. "What is the meaning of bioaccumulation as a measure of marine pollution effects?" pp.249-260. In: Concepts in Marine Pollution Measurements. H.H.White (ed). University of Maryland Sea Grant Program, College Park, MD.

Phelps, D.K., W. Galloway, F.P. Thurberg, E. Gould, and M.A. Dawson. 1981. "Comparison of several physiological monitoring techniques as applied to the blue mussel, Mytilus edulis, along a gradient of pollutant stress in Naragansett Bay, Rhode Island." pp. 335-355. In: Biological Monitoring of Marine Pollutants. F.J. Vernberg, A. Calabrese, F.P. Thurberg, and W.B. Vernberg. Academic Press, New York, NY.

Phillips, D.J.H. 1976. "The common mussel Mytilus edulis as an indicator of pollution by zinc, cadmium, lead, and copper. II. Relationship of metals in the mussel to those discharged by industry." Mar. Biol. 38:71-80.

Phillips, D.J.H. 1980. Quantitative aquatic biological indicators. Applied Science Publishers, Ltd., London, UK.

Phillips, D.J.H., and D.A. Segar. 1986. "Use of bio-indicators in monitoring conservative contaminants: programme design imperatives." Mar. Pollut. Bull. 17:10-17.

Pinkel, D. 1958. "The use of body surface area as a criterion of drug dosage in cancer chemotherapy." Cancer Res. 18:853-856.

Popham, J.D., D.C. Johnson, and J.M. D'Auria. 1980. "Mussels (Mytilus edulis) as "point source" indicators of trace metal pollution." Mar. Pollut. Bull. 11:261-263.

Puffer, H.W., M.J. Duda, and S.P. Azen. 1982. "Potential health hazards from consumption of fish caught in polluted coastal waters of Los Angeles County." N. Am. J. Fish. Manage. 2:74-79.

Puffer, H.W., and R.W. Gossett. 1983. "PCB, DDT, and benzo(a)pyrene in raw and pan-fried white croaker (Genyonemus lineatus)." Bull. Environ. Contam. Toxicol. 30:65-73.

Rapaport, R.A., and S.J. Eisenreich. 1984. "Chromatographic determination of octanol-water partition coefficients (K_{ows}) for the 58 PCB congeners." Environ. Sci. Technol. 18:163-170.

Rohde, C.A. 1976. "Composite sampling." Biometrics 32:278-282.

Rupp, E.M. 1980. "Age dependent values of dietary intake for assessing human exposure to environmental pollutants." Health Physics 39:151-163.

Russell, M., and M. Gruber. 1987. "Risk assessment in environmental policy-making." Science 236:286-290.

Saunders, S.D., and B. Petersen. 1987. Introduction to Tolerance Assessment System (TAS). Manuscript. U.S. Environmental Protection Agency, Office of Pesticide Programs, Washington, DC.

Schaeffer, D.J., H.W. Kerster, and K.G. Janardan. 1980. "Grab versus composite sampling: a primer for the manager and engineer." Environ. Manage. 4:157-163.

Schmitt, C.J. 1981. "Analysis of variance as a method for examining contaminant residues in fish: National Pesticide Monitoring Program." pp. 270-298. In: Aquatic Toxicology and Hazard Assessment Fourth Conference. D.R. Branson and K.L. Dickson (eds). ASTM STP 737. American Society for Testing and Materials, Philadephia, PA.

Skea, J.C. S. Jackling, J. Symula, H.A. Simonin, E.J. Harris, and J.R. Colquhoun. 1981. Summary of fish trimming and cooking techniques

used to reduce levels of oil soluble contaminants. New York Department of Environmental Conservation, Albany, NY. 36 pp.

Sloan, R.J., and E.G. Horn. 1986. "Contaminants in Hudson River striped bass: 1978-1985." Tech. Report No. 86-2. New York State Department of Environmental Conservation, Albany, NY.

Sloan, R., M. Brown, R. Brandt, and C. Barnes. 1985. "Hudson River PCFB relationships between resident fish, water, and sediment." Northeastern Environmental Science 3:138-152.

Smith, W.E., K. Funk, and M.E. Zabik. 1973. "Effects of cooking on concentrations of PCB and DDT compounds in chinook (Oncorhynchus tshawytscha) and coho (O. kisutch) salmon from Lake Michigan." J. Fish. Res. Board Can. 30:702-706.

Sonzogni, W.C., and W.R. Swain. 1984. "Perspectives on human health concerns from Great Lakes contaminants." pp. 1-29. In: Toxic Contaminants in the Great Lakes. J.O. Nriagu and M.S. Simmons (eds). Adv. in Environ. Sci. Technol. Series. No. 14. John Wiley and Sons, New York, NY.

SRI. 1980. Seafood consumption data analysis. Final Report. Prepared for U.S.Environmental Protection Agency, Office of Water Regulations and Standards, Washington, DC. SRI International, Menlo Park, CA. 44 pp.

Stara, J.F., R.C. Hertzberg, R.J.F. Bruins, M.L. Dourson, P.R. Durkin, L.S. Erdreich, and W.E. Pepelko. 1983. "Approaches to risk assessment of chemical mixtures." Report presented at the Second International Conference on Safety Evaluation and Regulation, Cambridge, MA. 23 pp.

Stich, H.F. (ed). 1982. "Carcinogens and mutagens in the environment." Vol. I. Food products. CRC Press, Boca Raton, FL.

Strong, C.R., and S.N. Luoma. 1981. "Variations in the correlation of body size with concentrations of Cu and Ag in the bivalve Macoma balthica." Can. J. Fish. Aquat. Sci. 38:1059-1064.

Suta, B.E. 1978. Human exposures to mirex and kepone. EPA-600/1-78-045. U.S. Environmental Protection Agency, Washington, DC.

Swain, W.R. 1988. "Human health consequences of consumption of fish contaminated with organochlorine compounds." Aquatic Toxicol. 11:357-377.

Tatken, R.L., and R.J. Lewis (eds). 1983. Registry of toxic effects of chemical substances 1981-1982 edition. 3 volumes. U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health, Cincinnati, OH.

Tetra Tech. 1985a. Bioaccumulation monitoring guidance: 1. estimating the potential for bioaccumulation of priority pollutants and 301(h) pesticides discharged into marine and estuarine waters. Final Report. Prepared for Office of Marine and Estuarine Protection, U.S. Environ-

mental Protection Agency, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 61 pp.

Tetra Tech. 1985b. Bioaccumulation monitoring guidance: 2. selection of target species and review of available bioaccumulation data. Final Report. Prepared for U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 52 pp. + 5 appendices.

Tetra Tech. 1985c. Bioaccumulation monitoring guidance: 3. recommended analytical detection limits. Final Report. Prepared for U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 23 pp.

Tetra Tech. 1986a. A framework for comparative risk analysis of dredged material disposal options. Final Report. Prepared for Resource Planning Associates for U.S. Army Corps of Engineers, Seattle District. Tetra Tech, Inc., Bellevue, WA. 94 pp. + 5 appendices.

Tetra Tech. 1986b. Bioaccumulation monitoring guidance: 5. strategies for sample replication and compositing. Final Report. Prepared for U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 46 pp.

Tetra Tech. 1986c. Elliott Bay toxics action program: initial data summaries and problem identification. Final Report. Prepared for the U.S. Environmental Protection Agency, Region 10. Tetra Tech, Inc., Bellevue, WA. 181 pp. + 8 appendices and maps.

Tetra Tech. 1986d. Technical support document for ODES statistical power analysis. Draft Report. Prepared for U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 28 pp.

Tetra Tech. 1986e. Bioaccumulation monitoring guidance: 4. analytical methods for U.S. EPA priority pollutants and 301(h) pesticides in tissues from estuarine and marine organisms. Final Report. Prepared for U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection, Washington, DC. Tetra Tech, Inc., Bellevue, WA.

Tetra Tech. 1986f. Quality assurance and quality control (QA/QC) for 301(h) monitoring programs guidance on field and laboratory methods. Final Report. Prepared for Marine Operations Division, Office of Marine and Estuarine Protection, U.S. Environmental Protection Agency, Washington, DC. Tetra Tech, Inc., Bellevue, WA. 267 pp. + appendices.

Thomann, R.V., and J.P. Connolly. 1984. "Model of PCB in the Lake Michigan lake trout food chain." Environ. Sci. Technol. 18:65-71.

Tollefson, L., and F. Cordle. 1986. "Methylmercury in fish: a review of residue levels, fish consumption and regulatory action in the United States." Environ. Health Perspectives 68:203-208.

Travis, C.C., S.A. Richter, E.A.C. Crouch, R. Wilson, and E.D. Klema. 1987. "Cancer risk management. A review of 132 federal regulatory decisions." Environ. Sci. Technol. 21:415-420.

U.S. Department of Agriculture. 1984. Agricultural statistics. U.S. Department of Agriculture, Washington, DC. p.506.

U.S. Environmental Protection Agency. 1980a. Ambient water quality criteria for polychlorinated biphenyls. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington, DC. 200 pp.

U.S. Environmental Protection Agency. 1980b. Water quality criteria documents; availability. U.S. EPA, Washington, DC. Federal Register, Vol.45, No.231, Part V. pp.79318-79379.

U.S. Environmental Protection Agency. 1981. Interim methods for the sampling and analysis of priority pollutants in sediments and fish tissue. EPA 600/4-81-055. U.S. Environmental Protection Agency, Environmental Monitoring and Support Laboratory, Cincinnati, OH.

U.S. Environmental Protection Agency. 1982. Method for use of caged mussels to monitor for bioaccumulation and selected biological responses of toxic substances in municipal wastewater discharges to marine waters. Draft. U.S. Environmental Protection Agency Env. Monitoring and Support Lab, Cincinnati, OH.

U.S. Environmental Protection Agency. 1984a. "Method 1625 Revision B. Semivolatile organic compounds by isotope dilution GC/MS." Federal Register Vol. 49, No. 209. October 26, 1984. pp. 43416-43429.

U.S. Environmental Protection Agency. 1984b. Risk assessment and management: framework for decision making. EPA 600/9-85-002. U.S. Environmental Protection Agency, Washington, DC. 35 pp.

U.S. Environmental Protection Agency. 1984c (revised January, 1985). U.S. EPA contract laboratory program statement of work for organics analysis, multi-media, multi-concentration. IFB WA 85-T176, T177, T178. U.S. Environmental Protection Agency, Washington, DC.

U.S. Environmental Protection Agency. 1985a. Health assessment document for 1,2-dichloroethane (ethylene dichloride). EPA/600/8-84/006F. Final Report. Office of Health and Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC. Table 9-66, pp. 9-253 to 9-256.

U.S. Environmental Protection Agency. 1985b. "National primary drinking water regulations; synthetic organic chemicals, inorganic chemicals and microorganisms; proposed rule." U.S. Environmental Protection Agency, Washington, DC. Federal Register. Vol.50, No.219, pp.46936-47022.

U.S. Environmental Protection Agency. 1985c. Contract laboratory program statement of work (SOW), inorganic analysis, multi-media, multi-concentration. SOW No. 785. U.S. Environmental Protection Agency, Washington, DC.

U.S. Environmental Protection Agency. 1986a. "Guidelines for carcinogen risk assessment." U.S. Environmental Protection Agency, Washington, DC. Federal Register, Vol.51, No. 185. pp.33992-34003.

U.S. Environmental Protection Agency. 1986b. "Guidelines for exposure assessment." U.S. Environmental Protection Agency, Washington, DC. Federal Register, Vol.51, No.185. pp.34042-34054.

U.S. Environmental Protection Agency. 1986c. "Guidelines for the health assessment of suspect developmental toxicants." U.S. Environmental Protection Agency, Washington, DC. Federal Register, Vol. 51, No. 185. pp. 34028-34040.

U.S. Environmental Protection Agency. 1986d. "Guidelines for the health risk assessment of chemical mixtures." U.S. Environmental Protection Agency, Washington, DC. Federal Register, Vol. 51, No.185. pp.34014-34025.

U.S. Environmental Protection Agency. 1986e. "Guidelines for mutagenicity risk assessment." U.S. Environmental Protection Agency, Washington, DC. Federal Register, Vol. 51, No. 185. pp. 34006-34012.

U.S. Environmental Protection Agency. 1986f. Superfund public health evaluation manual. EPA 540/1-86-060. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response, Washington, DC. 145 pp. + appendices.

U.S. Environmental Protection Agency. 1986g. Superfund Risk Assessment Information Directory. EPA 540/1-86/061. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response, Washington, DC.

U.S. Environmental Protection Agency. 1986h. Quality criteria for water. EPA 440/5-86-001. U.S. Environmental Protection Agency, Office of Water, Washington, DC.

U.S. Environmental Protection Agency. 1987a. Integrated Risk Information System (IRIS). Vol. I - Supportive Documentation EPA 600/8-86/032a, and Vol. II - Chemical Files EPA 600/8-86/032b. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Washington, DC.

U.S. Environmental Protection Agency. 1987b. Risk assessment, management, communication. A guide to selected sources. EPA IMSD/87-002. [Also First Update (EPA IMSD/87-002-a) and Second Update (EPA IMSD/87-002-b)]. U.S. Environmental Protection Agency, Office of Information Resources Management and Office of Toxic Substances, Washington, DC.

U.S. Fish and Wildlife Service. 1986. Type B technical information document: recommendations on use of habitat evaluation procedures and habitat suitability index models for CERCLA applications. Draft Report. U.S. Fish and Wildlife Service, Habitat Evaluation Procedures Work Group, Fort Collins, CO. 45 pp.

U.S. Food and Drug Administration. 1978. Pesticides analytical manual. Methods which detect multiple residues: foods and feeds. U.S. Food and Drug Administration, Washington, DC.

U.S. Food and Drug Administration. 1982. Levels for poisonous or deleterious substances in human food and animal feed. U.S. Food and Drug Administration, Washington, DC. 13 pp.

U.S. Food and Drug Administration. 1984. "Polychlorinated biphenyls (PCBs) in fish and shellfish; reduction of tolerances; final decision." U.S. Food and Drug Administration, Rockville, MD. Federal Register, Vol.49, No.100. pp.21514-21520.

U.S. Food and Drug Administration. 1986. Pesticides and industrial chemicals in domestic foods (FY 86). Compliance Program Guidance Manual. Programs 7304.004, 7304.004c, 7304.010. U.S. Food and Drug Administration, Washington, DC.

U.S. Office of Science and Technology Policy. 1985. "Chemical carcinogens; a review of the science and its associated principles." Federal Register, Vol.50. pp.10372-10442.

U.S.Office of Technology Assessment. 1979. Environmental contaminants in food. U.S.Office of Technology Assessment, Washington, DC. 229 pp.

U.S. Office of Technology Assessment. 1987. Identifying and regulating carcinogens. OTA-BP-H-42. U.S. Congress, Office of Technology Assessment, Washington, DC. 249 pp.

Vaessen, H.A.M.G., P.L. Schuller, A.A. Jekel, and A.A.M.M. Wibers. 1984. "Polycyclic aromatic hydrocarbons in selected foods: analysis and occurrence." Toxicol. Environ. Chem. 7:297-324.

Veith, G.D., N.M. Austin, and R.T. Morris. 1979a. "A rapid method for estimating log P for organic chemicals." Mar. Res. 13:43-47.

Veith, G.D., D.L. Defoe, and B.V. Bergstedt. 1979b. "Measuring and estimating the bioconcentration factor of chemicals in fish." J. Fish. Res. Board Can. 36:1046-1048.

Veith, G.D., K.J. Macek, S.R. Petrocelli, and J. Carroll. 1980. "An evaluation of using partition coefficients and water solubility to estimate bioconcentration factors for organic chemicals in fish." pp. 116-129. In: Aquatic Toxicology. ASTM STP 707. J.G. Eaton, P.R. Parrish, and A.C. Hendricks (eds). American Society for Testing and Materials, Philadelphia, PA.

Versar, Inc. 1985 Assessment of human health risk from ingesting fish and crab from Commencement Bay. EPA 910/9-85-129. Prepared for U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Versar, Inc., Springfield, VA.

Wagstaff, D.J., M. Meaburn, M. Bolger, S. Conrath, and B. Hackley. 1986. "Status of data sources on fish consumption in the United States." Mar. Fish. Rev. 48:20-23.

Whitmore, R.W. 1985. Methodology for characterization of uncertainty in exposure assessments. Final Report. OHEA-E-160. Office of Health and Environmental Assessment, Washington, DC. 44 pp.+ appendices.

Whittemore, A.S. 1983. "Facts and values in risk analysis for environmental toxicants." Risk Analysis 3:23-33.

Wilson, R., and E.A.C. Crouch. 1987. "Risk assessment and comparisons: an introduction." Science 236:267-270.

Appendix A

EPA/FDA Summary Policy Statement on Chemical Residues in Fish and Shellfish

This joint EPA/FDA policy statement outlines jurisdictional understandings relating to the regulation and control of poisonous or deleterious substances (chemical contaminants) in fish and shellfish and recommends procedures for improved interaction between the states and EPA/FDA headquarters and regional/district offices on these matters. The statement is intentionally written on a broad policy plane, primarily addressed to these governmental entities. More detailed, technical aspects are treated in the main text of this guidance manual.

The purpose of this statement is to:

- Clarify the respective roles and jurisdictions of EPA and FDA at the federal headquarters level and at the regional/district office level relating to regulation and monitoring of contaminated fish and shellfish (generically, referred to as "fish" below)
- Explain the differences between federal and state responsibilities and authorities in this area
- Establish procedures to improve federal-state communications on fish contamination issues
- Promote greater consistency between states in generating state health advisories on the consumption of contaminated fish.

Section I contains a brief description of the recent developments that make this statement particularly desirable at this time. Section II articulates the specific authorities and jurisdictions of EPA, FDA, and the states regarding contaminants in fish. Section III refers to the risk

assessment guidance on certain technical issues of toxicity and exposure given in the main text of this guidance manual and other guidance available from EPA and FDA. Section IV outlines a proposed Standing Committee established to facilitate information exchange, to deal with issues as they arise among the various jurisdictions, and to encourage greater consistency in assessments and advisories on chemical residues in fish.

Background

The protection of human health through the regulation and control of contaminated food stuffs is a joint federal and state responsibility. To do this job effectively requires that each party understand and respect the mandates and roles of the other.

The federal regulatory role is shared by FDA and EPA. FDA has direct enforcement responsibility over all contaminated food, including fish and shellfish that are shipped in interstate commerce. With respect to pesticides, as a part of its registration procedure, EPA is responsible for establishing tolerances (maximum permissible levels) for residues of pesticide chemicals that may be anticipated to appear in fish. Further, EPA is responsible for recommending, upon request from FDA, the appropriate action levels on pesticides which may become contaminants in food and for which a tolerance does not exist. FDA, by agreement with EPA, also enforces these action levels (Federal Register (FR) Vol. 39, No. 236, 42745, December 6, 1974).

Because of considerations involved in the establishment of federal action levels, such levels may or may not be directly applicable to the needs of the states when individual states attempt to evaluate the safety of the local consumption of fish by sports fishermen or others. When the states have sought federal advice from EPA or FDA offices for more detailed information beyond the simple statement of the tolerance or action level, that advice has not always been clear, consistent, and in accord with joint EPA/FDA policy.

The issue of consistency in decisionmaking has arisen more often in recent years as interest has broadened at both the federal and state level in the use of risk assessment as one tool in reaching decisions related to the consumption of contaminated fish. This trend is likely to continue. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) is making a number of site-specific decisions, pursuant to provisions of Superfund legislation, which deal with the possibility of pollutants in fish. Also, EPA regional offices are undertaking fish consumption risk assessments on a site- and area-specific basis in order to evaluate the human health impacts of site-specific regulatory decisions to control contamination sources. Additionally, more states are actively addressing the need to issue fish consumption advisories for local sports fishermen.

Therefore, it is important that federal agencies speak out as clearly as possible regarding their respective roles and that they establish procedures that will enable the states to obtain, in a timely manner, the information and advice they need in order to make decisions that impact on the health of their citizens.

Authority and Jurisdiction of EPA-FDA Over Contaminants in Fish

Much of the substance of this section is drawn from two preambles in the Federal Register (FR Vol. 39, No. 236, 42743-42748, December 6, 1974 and FR Vol. 47, No. 139, 42956-42958, September 29, 1982).

Statutes

The Federal Food, Drug and Cosmetics Act (FFDCA) is the principal authority for both EPA and FDA actions directly relating to the safety of fish as a human food source. Only under this Act can federal action be taken against contaminated fish moving in interstate commerce as being unsafe or unfit for human consumption.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) gives the EPA authority to deny registrations or cancel existing registrations for pesticide chemicals whose use would (or does) cause fish contamination to the extent that the risks of use of the pesticides exceed the benefits. FIFRA also provides EPA with authority to collect data on currently registered pesticides which may be causing fish contamination. The Toxic Substances Control Act (TSCA) can be used by EPA to regulate chemical substances to prevent such chemicals from becoming contaminants in fish or shellfish. EPA can also take action under RCRA or Superfund to prevent contamination of fish and shellfish caused by the release or anticipated release of hazardous substances.

Under the Clean Water Act (CWA), EPA publishes water quality criteria. The criteria, based upon the best scientific information available at the time and the Agency's published risk assessment procedures (FR Vol. 45, 79318-79379, November 28, 1980), assist the states in establishing water quality standards. A description of the EPA risk assessment procedures associated with contaminated fish can be found in the main text of this guidance manual.

Activities

EPA and FDA share the federal responsibility for the regulation of contaminants in foods that move in interstate commerce. Under the FFDCA, FDA has the primary federal role for assuring the safety of the food supply, including fish and shellfish. FDA is responsible for establishing safe levels for poisonous or deleterious substances (other than pesticide residues) that contaminate food [e.g., heavy metals, such as lead and mercury, and organics, such as polychlorinated biphenyls (PCBs)].

Under ideal conditions, FDA will attempt to establish a formal Section 406 tolerance limiting the extent of allowable contamination of a food. However, when toxicological data are scanty or conflicting, when additional data are being developed, or when other conditions are rapidly changing, the promulgation of a Section 406 tolerance may be inappropriate. Nevertheless, it may still be appropriate to take some regulatory action or to control exposure to a contaminant. In such circumstances, FDA may consider developing an action level under

authority of Sections 306, 402(a) and 406 of the FFDCA (FR Vol 39, No. 236, 42743-42748, December 6, 1974).

In practice, FDA's regulation of contaminants has proceeded more often through the use of action levels, rather than through formal tolerances. Existing action levels meet the same criteria as tolerances except they are intended for interim periods and can be instituted and changed more quickly than tolerances.

With respect to pesticide residues in food, EPA has the lead in establishing tolerances and recommending action levels. Under FIFRA, any pesticide used in the country must be registered for specific uses through procedures established by EPA. In addition, if the pesticide is registered for use in the production of food, it must also have a tolerance granted under FFDCA, limiting the amount of pesticide residue in food. These pesticide tolerances are set by EPA and are issued under the FFDCA for both raw agricultural commodities and processed foods. FDA is responsible for enforcing food tolerances. The use of action levels by EPA takes place in a somewhat different administrative context from that of FDA. EPA can recommend to FDA action levels on pesticide residues on foods to replace the formal FFDCA tolerances that are revoked along with cancellation of a pesticide registration in those cases in which the persistence of the pesticide in the environment makes some continuing residue in food unavoidable. EPA's criteria for establishing action levels are similar to FDA's, but they also consider crop groupings and Codex Alimentarious Commission recommendations (FR Vol. 47, No. 139, 42957, Sept 29, 1982).

Since 1971, action levels have been the result of close consultation between the two agencies. Because action levels are similar to tolerances in basis and effect and since EPA, under a 1971 Memorandum of Understanding between FDA and EPA was delegated responsibility for setting tolerances for pesticide contamination, EPA is responsible for recommending the appropriate level at which a pesticide action level is to be set. FDA is responsible for enforcing the action levels for pesticides.

Federal and State Distinctions

The authority of the FFDCA does not extend to fish that are not in interstate commerce. Accordingly, tolerances and action levels are typically established on a national basis when it is judged that a national problem exists for a particular contaminant. Thus, the federal authority is limited, and action levels are tailored to national needs and national patterns of consumption. For example, consumption levels of fish on a national per capita basis are generally considerably less than that typical of sports fishermen, or of most lakeshore or coastal regions of the U.S. Nonetheless, action levels or, more particularly, the toxicity information [Reference Dose, (RfD) or Acceptable Daily Intake (ADI)] that is considered in the setting of action levels may be useful to the states in establishing controls or advisories on local fish consumption that is outside the jurisdiction of the federal agencies. If a potential local health threat exists, a state or locality may wish to issue warnings or provide guidance on the quantity of contaminated fish which may be safely consumed, based on the best available toxicity

information and on assessment of the level of the contaminant found locally and on local fish consumption patterns.

It should also be understood that FFDCA permits the consideration of factors other than health and safety in the setting of nationally applicable levels. Action levels are predicated not only on safety but also on factors such as the economic impact likely to be experienced by affected members of the food industry in complying with the established levels. Therefore, particular risk management decisions made by the federal agencies in managing interstate commerce may not be in accord with, or take into consideration, the priorities of a particular state.

In several recent revocation actions of tolerances for cancelled pesticides (i.e., DDT, aldrin/dieldrin, and chlordane), a number of commenters raised concern about the EPA's decision not to recommend lower action levels for such pesticide residues in fish. The Agency concluded in its final rules revoking these tolerances that additional data were needed before the Agency could make its final recommendation on the fish action levels. It was recognized by the Agency that some population groups may be at higher risk because of the frequency and amount of fish consumed locally. However, setting an enforcement limit for this situation, while also satisfying the criteria for setting an appropriate national limit, is not usually possible. This is because action levels announced and enforced by FDA apply to fish in interstate commerce, and it would be very difficult, if not impossible, for FDA to enforce and defend in court differing regional limits.

States need to understand clearly the way federal action levels are developed if they are to adapt them to their local conditions or to extract from them the critical scientific information which is applicable generally and which would help to ensure a basic consistency in all state decisions. All of this makes it important that, when action levels are set, there be a clear distinction made between the risk assessment components and any risk management components, e.g. economic issues, and that there be a full explanation of any assumptions used in deriving the final levels.

As noted above, EPA takes enforcement and permit actions to protect against human exposure to toxic substances from specific emission sources and hazardous waste sites which can cause localized, intrastate impacts on public health and the environment. Analyses to support these regulatory actions include consideration of all exposure pathways, including fish consumption. When EPA (sometimes assisted by ATSDR) is the lead agency (in lieu of a state) for making site-specific decisions based on estimates of fish consumption risks (e.g., under CERCLA, TSCA Section 6(e), PCB Spill Cleanup Policy, etc.), the Agency also (1) advises the public of its findings and their relevance to EPA's regulatory actions to control specific sources, (2) notifies state and federal agencies of identified problems, and (3) recommends that states take action under their police powers to protect public health.

Risk Assessment Issues

The assessment of risks associated with the consumption of contaminated fish involves questions of toxicity; e.g.:

- Is the contaminant toxic? -- hazard identification
- How potent is the contaminant as a toxicant? -- dose-response assessment and questions of exposure; e.g.:
- What is the concentration of the pollutant in the fish?
- What is the extent of consumption of the fish by what populations?

Toxicity

Much of the information relevant to the first two questions above is available from either EPA or FDA and need not be generated by the states. For example, information on the toxicity of pesticides is available from EPA. Further, EPA has developed its Integrated Risk Information System (IRIS), which is a source of EPA risk assessment information on hundreds of chemicals accessible to the states by electronic-mail. The RfDs (ADIs) and carcinogenic potency factors found in IRIS, represent evaluations of a wide body of scientific literature, case-by-case judgments on difficult issues (e.g., the adequacy of the studies and their relevance to humans), and general science policy positions (e.g., the advisability of combining of benign and malignant tumors). In many cases, the agencies' toxicity evaluations and policy positions have benefited from widespread peer-review and scientific consensus at the national and international level. Such information should be directly useful to the states.

It should be noted that differences in approaches to risk assessment remain at the federal level. One area of particular interest is that of carcinogenicity risk assessment. To narrow the range of uncertainties and inconsistencies in this area as much as possible both EPA and FDA have officially adopted the "OSTP Cancer Principles" as the basis for their carcinogen risk assessments ("Chemical Carcinogens: A Review of the Science and its Associated Principles", OSTP 1985). These general principles were developed to provide interim guidance in areas of uncertainty until such time that additional scientific data provided the information needed to improve estimations of risk in human populations. The OSTP document was written in the light of the decisionmaking processes used by EPA and FDA and should be consulted for additional details. An application of the OSTP Principles to use at EPA can be found in the Agency's Guidelines for Cancer Risk Assessment (FR Vol. 51, 33992-34003, September 24, 1986).

Remaining differences between EPA and FDA in important risk assessment assumptions continue to be discussed and explored, both in discussions between staff members of the two agencies. The goal is to move toward a common position which has a firmer scientific basis. A detailed description of EPA's hazard identification and dose-response assessment processes for both cancer and non-cancer effects can be found in the main text of this guidance manual.

Exposure

The exposure information necessary to provide local answers to the latter two questions posed at the beginning of this section is the responsibility of federal agencies only when they have primary respon-

sibility for a site-specific investigation as is the case under TSCA and CERCLA which have not delegated substantial responsibility to the states. Even in these instances, data on the type and extent of local fish contamination and consumption can often best be gathered by the states.

In gathering and using the exposure information, there would be considerable merit in the states' using methods that are generally consistent with those used by the federal agencies. Such an approach would not only add to the credibility of state actions, but it also would facilitate the generation of coherent regulations or health advisories when different states share the same body of water.

A detailed discussion of factors to consider when planning sampling and analysis programs and making estimates of fish consumption can be found in the main text of this guidance manual.

Risk Management Issues: The Need For A Standing Committee

Governments at both the federal and state levels are committed to protecting public health and the environment. Within each level of government, various agencies have been assigned selected tasks directed toward this overall goal.

EPA has primary responsibility for identifying, correcting, and/or preventing environmental contamination. ATSDR is playing an increasingly important role in providing guidance in case-specific situations. FDA has a focused responsibility in protecting the portion of the food supply that moves in interstate commerce. The states have the responsibility of providing guidance or regulation at the more local level.

In order to achieve the overall goal--protection of public health and the environment--as expeditiously as possible, mechanisms should be established which foster mutual assistance and communication between agencies as they go about their interrelated tasks. At the federal level, EPA and FDA have been working together on action levels in fish for many years. In general, this association, set out in Congressional legislation and interagency Memoranda of Understanding over the years, is working smoothly to set enforceable standards for contaminants in fish in interstate commerce. However, areas of disagreement remain, and these sometime impede progress toward a common goal. Also, the EPA regions are appropriately becoming more active in risk assessment and in providing assistance to the states. With this regional involvement, there is a greater possibility for differences in interpretation and mixed responsibility when providing that assistance. In addition, the creation of ATSDR introduces another important participant at the federal level. At the state level, governmental agencies are increasingly aware of need for consistent guidance to their citizens. Particularly notable is the effort in the Great Lakes where, in cooperation with federal authorities, the eight affected states and the province of Ontario are making progress in issuing consistent health advisories regarding fish consumption. There is a need for a

mechanism which can address differences between these entities in specific cases and in general.

In addition, the federal government should do what it can to assist state efforts to achieve rational, consistent fish consumption advisories. Such assistance includes providing the best information available on the hazards posed by a chemical, specifically the hazard identification and dose-response assessment portions of the risk assessment. In addition, the federal agencies can be available to provide whatever advice might be sought by the states.

In order to mitigate the current difficulties which exist between the various governmental entities involved in contaminated fish issues, it is proposed that a Standing Committee on Fish Contamination be established, made up of representatives of EPA, FDA, ATSDR, and the states, possibly through the Association of State and Territorial Health Officials (ASTHO).

The purposes of the Committee would be the following:

- To work toward resolving any significant differences in the approaches used by agencies in assessing the risk associated with consumption of contaminated fish
- To provide the states with the appropriate information on hazard identification and dose-response assessment for contaminants in fish and to provide consistent interagency advice from the federal level when requested by the states
- To identify the need for federal action on contaminants found to be present in fish in several states
- To provide a forum in the instances requested by the states in which "early warning" information could be discussed and a coordinated response generated
- To provide for a common inter-institutional base of experience which would foster long term stability and consistency in fish contaminant related risk assessment generated by all of the governmental agencies involved.

EPA CONTACT ON RISK ASSESSMENT FOR FISH CONSUMPTION

Name	Organization	Phone	Subject Area
Dr. Renate Kimbrough	Office of Regional Operations	(202) 382-4727	EPA Coordination on Fish and Shell Fish FDA/EPA Standing Committee Chairman
Warren Banks	Office of Water Regulations and Standards	(202) 475-7893	
Michelle Hiller	Office of Marine and Estuarine Protection	(202) 475-7102	

Appendix B

Integrated Risk Information System (IRIS)

Overview of IRIS

The Integrated Risk Information System (IRIS), prepared and maintained by the U.S. Environmental Protection Agency (EPA), is an electronic data base containing health risk and EPA regulatory information on specific chemicals. IRIS was developed for EPA staff in response to a growing demand for consistent risk information on chemical substances for use in decision-making and regulatory activities. Although IRIS is designed for EPA staff, it is also accessible to state and local environmental health agencies. IRIS is available to libraries, private citizens, and other organizations by means of DIALCOM, Inc.'s Electronic Mail telecommunications system. The information in IRIS is intended for EPA staff without extensive training in toxicology, but with some knowledge of health sciences.

The heart of the IRIS system is its collection of computer files covering individual chemicals. These chemical files contain descriptive and quantitative information in the following categories:

- Oral and inhalation reference doses (RfDs) for chronic noncarcinogenic health effects
- Oral and inhalation slope factors and unit risks for chronic exposures to carcinogens
- Drinking water health advisories from EPA's Office of Drinking water
- EPA regulatory action summaries
- Supplementary data on acute health hazards and physical/chemical properties

To aid users in accessing and understanding the data in the IRIS chemical files, the following supportive documentation is provided:

- Alphabetical list of the chemical files in IRIS and list of chemicals by CAS (Chemical Abstracts Service) number.
- Background documents describing the rationales and methods used in arriving at the results shown in the chemical files.
- A user's guide that represents step-by-step procedures for using IRIS to retrieve chemical information.
- An example exercise in which the use of IRIS is demonstrated.
- Glossaries in which definitions are provided for the acronyms, abbreviations, and specialized risk assessment terms used in the chemical files and in the background documents.

Risk Assessment and Risk Management

The information in IRIS is intended for use in protecting public health through risk assessment and risk management. These two processes are briefly explained below.

Risk assessment has been defined as "the characterization of the potential adverse health effects of human exposures to environmental hazards" (NRC, 1983, p.18). In a risk assessment, the extent to which a group of people has been or may be exposed to a certain chemical is determined, and the extent of exposure is then considered in relation to the kind and degree of hazard posed by the chemical, thereby permitting an estimate to be made of the present or potential health risk to the group of people involved.

Risk assessment information is used in the risk management process in deciding how to protect public health. Examples of risk management actions include: deciding how much of a chemical a company may discharge into a river; determining which substances may be stored at a hazardous waste disposal facility; deciding to what extent a hazardous waste site must be cleaned up; setting permit levels for discharge, storage, or transport of hazardous waste; establishing levels for air emissions; and determining allowable levels of contamination in drinking water.

Essentially, risk assessment provides **information** on the health risk,, and risk management is the **action** taken based on that information.

A complete risk assessment consists of the following four steps:

1. Hazard identification,
2. Dose-response assessment,
3. Exposure assessment, and
4. Risk characterization,

with risk characterization being the transitional step to risk management.

The following discussion of the four steps of risk assessment was excerpted from "Principles of Risk Assessment: A Nontechnical Review" (U.S. EPA, 1985).

> Hazard identification involves gathering and evaluating data on the types of health injury or disease that may be produced by a chemical and on the conditions of exposure under which injury or disease is produced. It may also involve characterization of the behavior of a chemical within the body and the interactions it undergoes with organs, cells, or even part of cells. Data of the latter types may be of value in answering the ultimate question of whether the forms of toxicity known to be produced by a substance in one population group or in experimental settings are also likely to be produced in humans. Hazard identification is not risk assessment; we are simply determining whether it is scientifically correct to infer that toxic effects observed in one setting will occur in other settings (e.g., whether substances found to be carcinogenic or teratogenic in experimental animals are likely to have the same results in humans).
>
> Dose-response assessment involves describing the quantitative relationship between the amount of exposure to a substance and the extent of toxic injury or disease. Data are derived from animal studies, or less frequently, from studies in exposed populations. There may be many different toxic effects under different conditions of exposure.
>
> The risks of a substance cannot be ascertained with any degree of confidence unless dose-response relationships are quantified, even if the substance is known to be toxic.
>
> Exposure assessment involves describing the nature and size of the population exposed to a substance and the magnitude and duration of their exposure. The evaluation could concern past or current exposures, or exposures anticipated in the future.
>
> Risk characterization generally involves the integration of the assessment process (hazard identification, dose-response assessment, and exposure assessment) to determine the likelihood that humans will experience any of the various forms of toxicity associated with a substance. (In cases where exposure data are not available, hypothetical risk can be characterized by the integration of hazard identification and dose-response assessment data alone.) A framework to define the significance of the risk is developed, and all of the assumptions, uncertainties, and scientific judgments of the preceding three steps are presented.

The Role of IRIS in Risk Assessment/ Risk Management

IRIS is a tool that provides hazard identification and dose-response assessment information, but does not provide situational information on instances of exposure. **Combined with specific exposure information, the data in IRIS can be used for characterization of the public**

health risks of a given chemical in a given situation, which can then lead to risk management decision designed to protect public health.

The information contained in Section I (Chronic Health Hazard Assessment for Noncarcinogenic Effects) and Section II (Carcinogenicity Assessment for Lifetime Exposure) of the IRIS chemical files **represents a consensus judgment** of EPA's Reference Dose (RfD) Work Group or Carcinogen Risk Assessment Verification Endeavor (CRAVE) Work Group, respectively. These two Agency-wide work groups include high-level scientists from EPA's program offices (hazardous waste, air, pesticides) and the Office of Research and Development. Individual EPA offices have conducted comprehensive scientific reviews of the literature available on the particular chemical, and have performed the first two steps of risk assessment: hazard evaluation and dose-response assessment. These assessments have been summarized for IRIS and reviewed and revised by the appropriate work group. As new information becomes available, these work groups will re-evaluate their work and revise IRIS files accordingly. For more information, contact IRIS User Support in EPA's Environmental Criteria and Assessment Office, Cincinnati, OH (513/569-7254 or FTS 684-7254).

References

NRC (National Research Council), 1983. "The Nature of Risk Assessment." In: Risk Assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC. p. 18.

U.S. EPA. 1985. "Principles of Risk Assessment: A nontechnical review." Prepared for a risk assessment workshop. Easton, MD, March 17-18.

IRIS Questions and Answers

1) How can I get access to IRIS?
IRIS is available on every EPA electronic mailbox. Once the EPA electronic mail system has been accessed, simply type in 'IRIS' and hit the return key. The IRIS menu will appear on the screen. To obtain a copy of the IRIS User's Guide, call IRIS User Support at FTS 684-7254 or print out the identical on-line version provided in menu option 4.

2) How can those outside the agency get access to IRIS?
Those outside EPA can obtain an IRIS account by calling Mike McLaughlin of DIALCOM, Inc. at (202) 488-0550 or write to:

Mike McLaughlin
DIALCOM, Inc.
Federal Systems Division
600 Maryland Avenue SW
Washington, D.C. 20024

IRIS is also available through the Public Health Network (PHN) of the Public Health Foundation. Call Paul Johnson at (202)898-5600 for

more information. PHN is only available to local, state, and federal public health officials.

IRIS will be made available on the NIH National Library of Medicine's TOXNET system sometime during the late fall of 1989. At that time, call (301) 496-6531 for details.

3) How much does IRIS cost?
There is no charge to EPA users and the 47 states which have EPA-paid-for electronic mail accounts.

Those outside EPA who access IRIS through DIALCOM, Inc., must pay only for the cost of accessing IRIS. The user will be billed by DIALCOM, Inc. There is a $25.00 monthly minimum which is applied against a usage fee of $25.00 per hour. In addition to the usage fee, there is a $.05 charge per computer screen accessed. There is no EPA charge for using IRIS.

Those eligible to access IRIS via the Public Health Network will be charged under a different set of fees. Contact the Public Health Foundation at (202)898-5600 for more information.

4) Who do I call if I have a question about using IRIS?
Call IRIS User Support at (513) 569-7254 or FTS 684-7254.

5) Who do I call if I have a scientific or technical question about the reference doses?
Call the EPA Contact listed at the end of the reference dose section in the IRIS chemical file.

6) Who do I call if I have a scientific or technical question about the carcinogen (cancer) assessment?
Call the EPA Contact listed at the end of the carcinogen assessment section in the IRIS chemical file.

7) Who do I call if I have a scientific or technical question about drinking water health advisories?
Call the Safe Drinking Water Hotline at 1-800-426-4791.

8) Who do I call if I have a policy or general question about IRIS?
Call Rick Picardi at (202) 382-7315 or FTS 382-7315.

9) How can my organization get training in IRIS?
Call the IRIS contact for the appropriate EPA Region. The following are the contacts for the EPA Regions:

EPA Region		IRIS Contacts
I	Boston	Tom D'Avanzo (617) 565-3222 FTS 835-3222
II	New York	Marian Olson (212) 264-5682 FTS 264-5682

EPA Region		IRIS Contacts
III	Philadelphia	Roy Smith (215) 597-9857 FTS 597-9857
IV	Atlanta	Gayle Alston (404) 347-4216 FTS 257-4216
V	Chicago	David Dolan (312) 886-6195 FTS 886-6195
VI	Dallas	Fred Reitman (214) 655-2235 FTS 886-2235 Jill Lyons (214) 655-7208 FTS 255-7208
VII	Kansas City	Bob Fenemore (913) 236-2970 FTS 255-2970
VIII	Denver	Jim Baker (303) 293-1524 FTS 564-1524
IX	San Francisco	Arnold Den (415) 974-0906 FTS 454-0906
X	Seattle	Dave Tetta (206) 442-2138 FTS 399-2138 Dana Davoli (206) 442-2135 FTS 399-2135

10) When will (chemical name) be included in IRIS? When will the reference dose for (chemical name) be added to IRIS? When will the carcinogen assessment for (chemical name) be added to IRIS?
Call IRIS User Support at (513) 569-7254 or FTS 684-7254.

Use and Interpretation of The Data in IRIS

Lindane; CAS No. 58-89-9

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus

reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5.

Status of data for gamma-Hexachlorocyclohexane (gamma-HCH).

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/88
Inhalation RfD Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	pending	
Drinking Water Health Advisories (III.A.)	on-line	03/01/88
U.S. EPA Regulatory Actions (IV.)	on-line	03/01/88
Supplementary Data (V.)	on-line	01/31/87

I. CHRONIC HEALTH HAZARD ASSESSMENT FOR NONCARCINOGENIC EFFECTS

Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
Last Revised -- 03/01/88

The Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfDo)

I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Liver and kidney toxicity Rat, Subchronic Oral Bioassay Zoecon Corp., 1983	NOAEL: 4 ppm diet 3 (m/kg/day females) LOAEL: 20 ppm diet (1.55 mg/kg/day males)	1000	1	3E-4 mg/kg/day

*Dose Conversion Factors & Assumptions: Converted dose calculated from actual food consumption data

I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)
Twenty male and 20 female Wistar KFM-Han (outbred) SPF rats/treatment group were administered 0, 0.2, 0.8, 4, 20, or 100 ppm lindane (99.85%) in the diet. After 12 weeks, 15 animals/sex/group were sacrificed. The remaining rats were fed the control diet for an additional 6 weeks before sacrifice. No treatment-related effects were noted on mortality, hematology, clinical chemistry, or urinalysis. Rats receiving 20 and 100 ppm lindane were observed to have greater-than-control incidence of the following: liver hypertrophy, kidney tubular degeneration, hyaline droplets, tubular distension, interstitial nephritis, and basophilic tubules. Since these effects were mild or rare in animals receiving 4 ppm, this represents a NOAEL. The reviewers of the study calculated the dose to be 0.29 mg/kg/day for males and 0.33 mg/kg/day for females, based on measured food intake.

In a 2-year feeding study (Fitzhugh, 1950), 10 Wistar rats/sex/group were exposed to 5, 10, 50, 100, 400, 800, or 1600 ppm lindane. Slight liver and kidney damage and increased liver weights were noted at the 100 ppm level. If a food intake equal to 5% body weight is assumed, a NOAEL of 2.5 mg/kg bw/day (50 ppm) can be determined from this assay. In a 2-year bioassay (Rivett et al., 1978), four beagle dogs/sex/group were administered 0, 25, 50, or 100 ppm lindane in the diet. Treatment-related effects noted in the animals of the 100 ppm group were increased serum alkaline phosphatase and enlarged dark friable livers. A NOAEL was determined to be 50 ppm (1.6 mg/kg bw/day).

I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)
UF = 1000. A factor of 10 each was employed for use of a subchronic vs. a lifetime assay, to account for interspecies variation and to protect sensitive human subpopulations.
MF = 1

I.A.4. ADDITIONAL COMMENTS (ORAL RfD)
Data on reproductive effects of lindane are inconclusive. Most reports indicate that hexachlorocyclohexane isomers are nonteratogenic.

I.A.5. CONFIDENCE IN THE ORAL RfD
Study: Medium
Data Base: Medium
RfD: Medium
The principal study used an adequate number of animals and measured multiple endpoints. Since there are other reported chronic and subchronic studies, confidence in the data base is medium. Medium confidence in the RfD follows.

I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD
U.S. EPA. 1985. Drinking Water Criteria Document for Lindane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. The RfD in the Drinking Water Criteria Document has been extensively reviewed by U.S. EPA scientists and selected outside experts.

Agency RfD Work Group Review: 01/22/86
Verification Date: 01/22/86

I.A.7. EPA CONTACTS (ORAL RfD)
Michael L. Dourson / ORD -- (513)569-7544 / FTS 684-7544
Christopher T. DeRosa / ORD -- (513)569-7534 / FTS 684-7534

I.B. REFERENCE DOSE FOR CHRONIC INHALATION EXPOSURE (RfDi)
Not available at this time

II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE
Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
This chemical is among those substances evaluated by the U.S. EPA for evidence of human carcinogenic potential. This does not imply that this chemical is necessarily a carcinogen. The evaluation for this chemical is under review by an inter-office Agency work group. A risk assessment summary will be included on IRIS when the review has been completed.

III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS
Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
Last Revised -- 03/01/88

III.A. DRINKING WATER HEALTH ADVISORIES
The Office of Drinking Water provides Drinking Water Health Advisories (HAs) as technical guidance for the protection of public health. HAs are not enforceable Federal standards. HAs are concentrations of a substance in drinking water estimated to have negligible deleterious effects in humans, when ingested, for a specified period of time. Exposure to the substance from other media is considered only in the derivation of the lifetime HA. Given the absence of chemical-specific data, the assumed fraction of total intake from drinking water is 10% for inorganic contaminants and 20% for organic contaminants. The lifetime HA is calculated from the Drinking Water Equivalent Level (DWEL) which, in turn, is based on the Oral Chronic Reference Dose. Lifetime HAs are not derived for compounds which are potentially carcinogenic for humans because of the difference in assumptions concerning toxic threshold for carcinogenic and noncarcinogenic effects. A more detailed description of the assumptions and methods used in the derivation of HAs is provided in Background Document 3 in Service Code 5.

III.A.1. ONE-DAY HEALTH ADVISORY FOR A CHILD
Appropriate data for calculating a One-day HA are not available. It is recommended that the Ten-day HA of 1.2 mg/L (rounded to 1 mg/L) be used as the One-day HA.

III.A.2. TEN-DAY HEALTH ADVISORY FOR A CHILD
Ten-day HA -- 1.2E+0 mg/L

NOAEL -- 12.3 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability)
Assumptions -- 1 L/day water consumption for a 10-kg child
Principal Study -- Muller et al., 1981
Rats were fed lindane at daily doses of 1.3, 12.3, or 25.4 mg/kg bw in the diet for 30 days. Nerve conduction delay was observed in the animals fed a daily dose of 25.4 mg/kg but was not observed at dose levels of 12.3 or 1.3 mg/kg. A NOAEL of 12.3 mg/kg/day was identified.

III.A.3. LONGER-TERM HEALTH ADVISORY FOR A CHILD
Longer-term (Child) HA -- 3.3E-2 mg/L
NOAEL -- 0.33 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 1 L/day water consumption for a 10-kg child
Principal Study -- Zoecon Corporation, 1983
Male and female rats were fed lindane at dietary levels of 0, 0.2, 0.8, 4, 20, or 100 ppm for 84 consecutive days. Liver hypertrophy, kidney tubular degeneration, hyaline droplets, tubular casts, tubular distension, interstitial nephritis, and basophilic tubules were observed in the 20 and 100 ppm groups. Effects were rare and very mild when noted at 4 ppm. The NOAEL was considered to be 4 ppm in this study. Based upon measured food consumption, the daily intake of lindane at 4 ppm in the diet was 0.29 mg/kg in males and 0.33 mg/kg in females. The dose of 0.33 mg/kg is identified as the NOAEL.

III.A.4. LONGER-TERM HEALTH ADVISORY FOR AN ADULT
Longer-term (Adult) HA -- 1.2E-1 mg/L
NOAEL -- 0.33 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study) Assumptions -- 2 L/day water consumption for a 70-kg adult
Principal Study -- Zoecon Corporation, 1983 (study described in III.A.3.)

III.A.5. DRINKING WATER EQUIVALENT LEVEL / LIFETIME HEALTH ADVISORY
DWEL -- 1E-2 mg/L
Assumptions -- 2 L/day water consumption for a 70-kg adult
RfD Verification Date -- 01/22/86 (see Section I.A. of this file)
Lifetime HA -- 2E-4 mg/L
Assumptions -- 20% exposure by drinking water
Principal Study -- Zoecon Corporation, 1983 (This study was used in the derivation of the chronic oral RfD; see Section I.A.2.) NOTE: A safety factor of 10 was used in the derivation of this HA, in addition to the UF of 1000 for the RfD, to account for the possible carcinogenicity of this substance. The assessment for the potential human carcinogenicity of lindane is currently under review.

III.A.6. ORGANOLEPTIC PROPERTIES
No data available

III.A.7. ANALYTICAL METHODS FOR DETECTION IN DRINKING WATER
Determination of lindane is by a liquid-liquid extraction gas chromatographic procedure.

III.A.8. WATER TREATMENT

Treatment techniques capable of removing lindane from drinking water include adsorption on activated carbon, air stripping, reverse osmosis, and oxidation.

III.A.9. DOCUMENTATION AND REVIEW OF HAs

Muller, D., H. Klepel, R.M. Macholz, H.J. Lewerenz and R. Engst. 1981.
"Electroneurophysiological studies on neurotoxic effects of hexachlorocyclo-hexane isomers and gamma-pentachlorocyclohexene." Bull. Environ. Contam. Toxicol. 27(5): 704-706. Zoecon Corporation. 1983. MRID No. 00128356.
Available from EPA. Write to FOI, EPA, Washington D.C. 20460.
U.S. EPA. 1985. Final Draft of the Drinking Water Criteria Document on Lindane. Office of Drinking Water, Washington, DC.
EPA review of HAs in 1985.
Public review of HAs following notification of availability in October, 1985. Scientific Advisory Panel review of HAs in June, 1986.
Preparation date of this IRIS summary -- 06/17/87

III.A.10. EPA CONTACTS

Yogendra Patel / ODW -- (202)382-7585 / FTS 382-7585
Edward V. Ohanian / ODW -- (202)382-7571 / FTS 382-7571

III.B. OTHER ASSESSMENTS

Content to be determined

IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
Last Revised -- 03/01/88
EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

IV.A. CLEAN AIR ACT (CAA)

No data available

IV.B. SAFE DRINKING WATER ACT (SDWA)

IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 0.0002 mg/L (Proposed, 1985)
Considers technological or economic feasibility? -- NO

Discussion -- An MCLG of 0.0002 mg/L for lindane is proposed based upon a provisional DWEL of 0.01 mg/L and an assumed drinking water contribution of 20%. A DWEL of 0.01 mg/L was calculated from a NOAEL of 0.3 mg/kg/day in rats (feeding study) with an uncertainty factor of 1000 and a consumption of 2 L of water/day. Reference -- 50 FR 46936 Part IV (11/13/85)
EPA Contact -- Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water
Value (status) -- 0.004 mg/L (Interim, 1980)
Considers technological or economic feasibility? -- NO
Reference -- 45 FR 57332 (08/27/80)
EPA Contact -- Yogendra Patel / Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

IV.C. CLEAN WATER ACT (CWA)

IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health
Water and Fish Consumption: 1.86E-2 ug/L
Fish Consumption Only: 6.25E-2 ug/L
Considers technological or economic feasibility? -- NO
Discussion -- For the maximum protection from the potential carcinogenic properties of this chemical, the ambient concentration should be zero. However, zero may not be attainable at this time so the criteria given represent a E-6 incremental increase in cancer risk over a lifetime.
Reference -- 45 FR 79318 (11/28/80)
EPA Contact -- Criteria and Standards Division, OWRS (202)475-7315 / FTS 475-7315

IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms
Freshwater:
Acute -- 2.0E+0 ug/L
Chronic -- 8.0E-2 ug/L
Marine:
Acute -- 1.6E-1 ug/L
Chronic -- None
Considers technological or economic feasibility? -- NO
Discussion -- Water quality criteria for the protection of aquatic life are derived from a minimum data base of acute and chronic tests on a variety of aquatic organisms. The data are assumed to be statistically representative and are used to calculate concentrations which will not have significant short- or long-term effects on 95% of the organisms exposed. Recent criteria (1985 and later) contain duration and frequency stipulations: the acute criteria maximum concentration is a 1-hour average and the chronic criteria continuous concentration is a 4-day average which are not to be exceeded more than once every 3 years, on the average (see Stephen et al., 1985). Earlier criteria (1980-1984) contained instantaneous acute and 24-hour average chronic

concentrations which were not to be exceeded. The freshwater chronic WQC is a 24-hour average.
Reference -- 45 FR 79318 (11/28/80)
EPA Contact -- Criteria and Standards Division, OWRS
(202)475-7315 / FTS 475-7315

IV.D. FEDERAL INSECTICIDE FUNGICIDE AND RODENTICIDE ACT (FIFRA)

IV.D.1. PESTICIDE ACTIVE INGREDIENT, Registration Standard
Status -- Issued (1985)
Reference -- Lindane Pesticide Registration Standard. Current, 1985.
EPA Contact -- Registration Branch, OPP / (703)557-7760 / FTS 557-7760

IV.D.2. PESTICIDE ACTIVE INGREDIENT, Special Review
Action -- Final regulatory action - PD4 (1984)
Considers technological or economic feasibility? -- YES
Summary of regulatory action -- Negotiated settlements have been made for Lindane in dog dips [49 FR 26282 (06/27/84)] and in smoke bombs [50 FR 5424 (02/08/85)].
Reference -- 45 FR 48513 (10/19/83); 49 FR 26282 (06/27/84)
EPA Contact -- Special Review Branch, OPP / (703)557-7400 / FTS 557-7400

IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)
No data available

IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

Status -- Listed
Reference -- 52 FR 25942 (07/09/87)
EPA Contact -- Jerry Garman / OSW / (202)382-4658 / FTS 382-4658

IV.G. SUPERFUND (CERCLA)
IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment
Value (status) -- 1 pound (Statutory, 1987)
Considers technological or economic feasibility? -- NO
Discussion -- The 1-pound RQ for lindane is based on aquatic toxicity as assigned by Section 311(b)(4) of the Clean Water Act (40 CFR 117.3). Available data indicate a 96-hour Median Threshold Limit of ppm, which corresponds to an RQ of 1 pound.
Reference -- 52 FR 8140 (03/16/87)
EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

V. SUPPLEMENTARY DATA
Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
Last Revised -- 01/31/87
The information contained in this section (subsections A and B) has been extracted from the EPA Chemical Profiles Database, which has been compiled from a number of secondary sources and has not

undergone formal Agency review. The complete reference listings for the citations in this section are provided in Service Code 5. The user is urged to read Background Document 5 in Service Code 5 for further information on the sources and limitations of the data presented here.

V.A. ACUTE HEALTH HAZARD INFORMATION

Toxicity -- Lindane is a stimulant of the nervous system, causing violent convulsions that are rapid in onset and generally followed by death or recovery within 24 hours (Hayes, 1982, p. 218). The probable human oral lethal dose is 50-500 mg/kg, or between 1 teaspoon and 1 ounce for a 150-lb (70 kg) person (Gosselin et al., 1984, p. II-286).
Medical Conditions Generally Aggravated by Exposure -- Not Found
Signs and Symptoms of Exposure -- Contact with eyes or skin may produce irritation (DASE, 1980, p. 529). Vomiting, faintness, tremor, restlessness, muscle spasms, unsteady gait, and convulsions may occur as a result of exposure. Elevated body temperature and pulmonary edema have been reported in children. Coma, respiratory failure, and death can result. Exposure to vapors of this compound or its thermal decomposition products may lead to headache, nausea, vomiting, and irritation of the eyes, nose, and throat (Gosselin et al., 1984, pp. III-240, 241).

V.B. PHYSICAL-CHEMICAL PROPERTIES

Chemical Formula -- C6H6Cl6 (Weast 1979, p. C-262)
Molecular Weight -- 290.83 (Weast 1979, p. C-262)
Boiling Point -- 614F, 323.4C (Weast, 1979, p. C-262); Decomposes (NIOSH/OSHA, 1978, p. 120)
Specific Gravity (H2O = 1) -- 1.9 (DASE, 1980, p. 529)
Vapor Pressure (mmHg) -- 9.4 x 10-6 at 20C (Merck, 1983, p. 789)
Melting Point -- 234.5F, 112.5C (Weast, 1979, p. C-262)
Vapor Density (AIR = 1) -- Not Found
Evaporation Rate (Butyl acetate = 1) -- Not Found
Solubility in Water -- Insoluble (Weast, 1979, p. C-262)
Flash Point (Method Used) -- Not Found
Flammable Limits:
LEL -- Not Found
UEL -- Not Found
Appearance and Odor -- Colorless solid with a musty odor; pure material is odorless (NIOSH/OSHA, 1978, p. 120).
Conditions to Avoid -- Not Found
Hazardous Decomposition or Byproducts -- Thermal decomposition products may include chlorine, hydrochloric acid, and phosgene (Sax, 1984, p. 366). Use -- Lindane is used as a pesticide (Hawley, 1981, p. 617) and scabicide (Hayes, 1982, p. 221).

VI. REFERENCES

Substance Name -- gamma-Hexachlorocyclohexane (gamma-HCH)
Primary Synonym -- Lindane
CASRN -- 58-89-9
Not available at this time

SYNONYMS: cyclohexane, 1,2,3,4,5,6-hexachloro-, gamma-isomer; aalindan; aficide; agrisol g-20; agrocide; agrocide 2; agrocide 7; agrocide 6g; agrocide iii; agrocide wp; agronexit; ameisenatod; ameisenmittel merck; aparasin; aphtiria; aplidal; arbitex; bbh; benhex; bentox 10; benzene hexachloride-gamma-isomer; gamma-ben-

zene hexachloride; bexol; bhc; gamma-bhc; celanex; chloresene; codechine; dbh; detmol-extrakt; detox 25; devoran; dol granule; drill tox-spezial aglukon; ent 7,796; entomoxan; exagama; forlin; gallogama; gamacarbatox; gamacid; gamaphex; gamene; gamiso; gamma-col; gammahexa; gammahexane; gammalin; gammalin 20; gammaterr; gammex; gammexane; gammopaz; gexane; hcch; hch; gamma-hch; heclotox; hexa; gamma-hexachlor; hexachloran; gamma-hexachloran; hexachlorane; gamma-hexachlorane; gamma-hexachlorobenzene; 1-alpha,2-alpha,3-beta,4-alpha,5-alpha,6-beta-hexachlorocyclohexane; gamma-hexachlorocyclohexane; 1,2,3,4,5,6-hexachlorocyclohexane; gamma-1,2,3,4,5,6-hexachlorocyclohexane; hexachlorocyclohexane, gamma-isomer; 1,2,3,4,5,6-hexachlorocyclohexane, gamma-isomer; hexatox; hexaverm; hexicide; hexyclan; hgi; hortex; inexit; isotox; jacutin; kokotine; kwell; lendine; lentox; lidenal; lindafor; lindagam; lindagrain; lindagranox; lindane; gamma-lindane; lindane (acgih,dot); lindapoudre; lindatox; lindosep; lintox; lorexane; milbol 49; mszycol; na 2761 (dot); nci-c00204; neo-scabicidol; nexen fb; nexit; nexit-stark; nexol-e; nicochloran; novigam; omnitox; ovadziak; owadziak; pedraczak; pflanzol; quellada; rcra waste number u129; sang gamma; silvanol; spritz-rapidin; spruehpflanzol; streunex; tap 85; tri-6; viton

List of Chemicals on IRIS (Alphabetical Order)

The following is a list of chemicals on IRIS. The list is in alphabetical order by the chemical name used on IRIS. If you do not find your chemical of interest listed here look for the Chemical Abstracts Service Registry Number (CASRN) in the CASRN listing.

Sections Available:
RfD = Chronic noncarcinogenic assessment (Reference Dose)
CAR = Chronic carcinogenicity assessment
HA = Drinking Water Health Advisories

Chemical	CASRN	RfD	CAR	HA
Acetone	67-64-1	●		
Acetonitrile	75-05-8	●		
Acrylic Acid	79-10-7	●		
Acrylonitrile	107-13-1		●	
Alachlor	15972-60-8	●		●
Aldicarb	116-06-3	●		●
Aldrin	309-00-2	●	●	
Allyl Alcohol	107-18-6	●		
Aluminum Phosphide	20859-73-8	●		
Amdro	67485-29-4	●		
Ametryn	834-12-8	●		
Ammonium Sulfamate	7773-06-0	●		
Antimony	7440-36-0	●		
Apollo	74115-24-5	●		
Arsenic, inorganic	7440-38-2		●	
Atrazine	1912-24-9	●		
Barium	7440-39-3	●		
Barium Cyanide	542-62-1	●		

Chemical	CASRN	RfD	CAR	HA
Baygon	114-26-1	●		
Bayleton	43121-43-3	●		
Baythroid	68359-37-5	●		
Benefin	1861-40-1	●		
Benomyl	17804-35-2	●		
Bentazon	25057-89-0	●		
Benzene	71-43-2		●	●
Benzidine	92-87-5		●	
Benzo[a]pyrene (BaP)	50-32-8		●	
Beryllium	7440-41-7	●		
Bidrin	141-66-2	●		
1,1-Biphenyl	92-52-4	●		
Bis(2-ethylhexyl)phthalate (BEHP)	117-81-7	●		
Bis(chloroethyl)ether (BCEE)	111-44-4		●	
Bromodichloromethane	75-27-4	●		
Bromoform	75-25-2	●		
Bromomethane	74-83-9	●		
Bromoxynil octanoate	1689-99-2	●		
1,3-Butadiene	106-99-0		●	
n-Butanol	71-36-3	●		
Butylate	2008-41-5	●		
Butylphthalyl Butylglycolate (BPBG)	85-70-1	●		
Cadmium	7440-43-9		●	
Calcium Cyanide	592-01-8	●		
Captafol	2425-06-1	●		
Captan	133-06-2	●		
Carbaryl	63-25-2	●		
Carbofuran	1563-66-2	●		●
Carbon Disulfide	75-15-0	●		
Carbon Tetrachloride	56-23-5	●	●	●
Carbosulfan	55285-14-8	●		
Carboxin	5234-68-4	●		
Chloramben	133-90-4	●		
Chlordane	57-74-9	●	●	●
Chlorine Cyanide	506-77-4	●		
Chloroform	67-66-3	●		
Chloromethyl Methyl Ether (CMME)	107-30-2		●	
Chlorothalonil	1897-45-6	●		
Chlorpyrifos	2921-88-2	●		
Chlorsulfuron	64902-72-3	●		
Chromium(III)	16065-83-1	●		●
Chromium(VI)	7440-47-3	●	●	●
Copper cyanide	544-92-3	●		
Cyanazine	21725-46-2	●		
Cyanide, free	57-12-5	●		●
Cyanogen	460-19-5	●		
Cyclohexanone	108-94-1	●		
Cyromazine	66215-27-8	●		
Dalapon, sodium salt	75-99-0	●		
Danitol	39515-41-8	●		
Decabromodiphenyl Ether (DBDPE)	1163-19-5	●		
Demeton	8065-48-3	●		
1,4-Dibromobenzene	106-37-6	●		

Chemical	CASRN	RfD	CAR	HA
Dibromochloromethane	124-48-1	●		
Dibutyl phthalate	84-74-2	●		
Dicamba	1918-00-9	●		
Dichlorodifluoromethane	75-71-8	●		
p,p'-Dichlorodiphenyltrichloroethane (DDT)	50-29-3	●		
1,2-Dichloroethane	107-06-2		●	●
1,1-Dichloroethylene	75-35-4	●	●	
Dichloromethane	75-09-2	●	●	●
2,4-Dichlorophenol	120-83-2	●		
4-(2,4-Dichlorophenoxy)butyric acid (2,4-DB)	94-82-6	●		
2,4-Dichlorophenoxyacetic acid (2,4-D)	94-75-7	●		
1,3-Dichloropropene	542-75-6	●		
Dichlorvos	62-73-7	●		
Diethyl phthalate	84-66-2	●		
Diflubenzuron	35367-38-5	●		
Dimethipin	55290-64-7	●		
Dimethoate	60-51-5	●		
Dimethyl Terephthalate (DMT)	120-61-6	●		
N-N-Dimethylaniline	121-69-7	●		
2,4-Dinitrophenol	51-28-5	●		
Dinoseb	88-85-7	●		
Diphenamid	957-51-7	●		
Diphenylamine	122-39-4	●		
1,2-Diphenylhydrazine	122-66-7		●	
Diquat	85-00-7	●		
Disulfoton	298-04-4	●		
Diuron	330-54-1	●		
Dodine	2439-10-3	●		
Endosulfan	115-29-7	●		
Endothall	145-73-3	●		
Epichlorohydrin	106-89-8	●	●	●
Ethion	563-12-2	●		
Ethyl Acetate	141-78-6	●		
S-Ethyl dipropylthiocarbamate (EPTC)	759-94-4	●		
Ethyl p-nitrophenyl phenylphosphorothioate (EPN)	2104-64-5	●		
Ethylbenzene	100-41-4	●		●
Ethylene Glycol	107-21-1	●		
Ethylphthalyl Ethylglycolate (EPEG)	84-72-0	●		
Fenamiphos	22224-92-6	●		
Fluometuron	2164-17-2	●		
Fluorine (soluble fluoride)	7782-41-4	●		
Fluridone	59756-60-4	●		
Folpet	133-07-3	●		
Fonofos	944-22-9	●		
Formic Acid	64-18-6	●		
Fosetyl-al	39148-24-8	●		
Furan	110-00-9	●		
Glufosinate-ammonium	77182-82-2	●		
Glyphosate	1071-83-6	●		

Chemical	CASRN	RfD	CAR	HA
Heptachlor	76-44-8	●	●	●
Heptachlor Epoxide	1024-57-3	●	●	●
Hexabromobenzene	87-82-1	●		
Hexachlorobutadiene	87-68-3	●	●	
alpha-Hexachlorocyclohexane (alpha-HCH)	319-84-6		●	
beta-Hexachlorocyclohexane (beta-HCH)	319-85-7		●	
delta-Hexachlorocyclohexane (delta-HCH)	319-86-8		●	
epsilon-Hexachlorocyclohexane (epsilon-HC)	6108-10-7		●	
gamma-Hexachlorocyclohexane (gamma-HCH)	58-89-9	●		●
technical Hexachlorocyclohexane (t-HCH)	608-73-1		●	
Hexachlorocyclopentadiene (HCCPD)	77-47-4	●		
Hexachlorodibenzo-p-dioxin, mixture (HxCDD)	19408-74-3		●	
Hexachloroethane	67-72-1	●	●	
Hexazinone	51235-04-2	●		
Hydrogen Cyanide	74-90-8	●		●
Hydrogen Sulfide	7783-06-4	●		
Imazalil	35554-44-0	●		
Imazaquin	81335-37-7	●		
Isobutyl Alcohol	78-83-1	●		
Isophorone	78-59-1	●		
Isopropalin	33820-53-0	●		
Lead and compounds (inorganic)	7439-92-1	●		
Linuron	330-55-2	●		
Londax	83055-99-6	●		
Malathion	121-75-5	●		
Maleic Hydrazide	123-33-1	●		
Metalaxyl	57837-19-1	●		
Methamidophos	10265-92-6	●		
Methomyl	16752-77-5	●		
Methyl Ethyl Ketone (MEK)	78-93-3	●		
Methyl Isobutyl Ketone (MIBK)	108-10-1	●		
Methyl Mercury	22967-92-6	●		
Methyl Parathion	298-00-0	●		
2-(2-Methyl-4-chlorophenoxy) propionic acid (MCPP)	93-65-2	●		
2-Methyl-4-chlorophenoxyacetic acid (MCPA)	94-74-6	●		
Metolachlor	51218-45-2	●		
Metribuzin	21087-64-9	●		
Mirex	2385-85-5	●		
Naled	300-76-5	●		
Nickel Carbonyl	13463-39-3		●	
Nickel Refinery Dust	00-02-0		●	
Nickel Subsulfide	12035-72-2		●	

Chemical	CASRN	RfD	CAR	HA
Nickel, soluble salts	7440-02-0	●		
Nitrapyrin	1929-82-4	●		
Nitrate	14797-55-8	●		●
Nitric Oxide	10102-43-9	●		
Nitrite	14797-65-0	●		●
Nitrobenzene	98-95-3	●		
Nitrogen Dioxide	10102-44-0	●		
N-Nitroso-di-n-butylamine	924-16-3		●	
N-Nitroso-N-methylethylamine	10595-95-6		●	
N-Nitrosodi-N-propylamine	621-64-7		●	
N-Nitrosodiethanolamine	1116-54-7		●	
N-Nitrosodiethylamine	55-18-5		●	
N-Nitrosodimethylamine	62-75-9		●	
N-Nitrosodiphenylamine	86-30-6		●	
N-Nitrosopyrrolidine	930-55-2		●	
Norflurazon	27314-13-2	●		
Octabromodiphenyl ether	32536-52-0	●		
Oryzalin	19044-88-3	●		
Oxadiazon	19666-30-9	●		
Oxamyl	23135-22-0	●		●
Oxyfluorfen	42874-03-3	●		
Paclobutrazol	76738-62-0	●		
Paraquat	1910-42-5	●		
Pentabromodiphenyl ether	32534-81-9	●		
Thallic oxide	1314-32-5	●		
Thallium acetate	563-68-8	●		
Thallium carbonate	6533-73-9	●		
Thallium chloride	7791-12-0	●		
Thallium nitrate	10102-45-1	●		
Thallium selenite	12039-52-0	●		
Thallium(I) sulfate	7446-18-6	●		
Thiobencarb	28249-77-6	●		
Thiophanate-methyl	23564-05-8	●		
Thiram	137-26-8	●		
Toluene	108-88-3	●		
Triallate	2303-17-5	●		
1,2,4-Tribromobenzene	615-54-3	●		
1,1,2-Trichloro-1,2,2-trifluoroethane (CFC-113)	76-13-1	●		
1,2,4-Trichlorobenzene	120-82-1	●		
1,1,1-Trichloroethane	71-55-6	●		
1,1,2-Trichloroethane	79-00-5	●	●	
Trichloroethylene	79-01-6		●	
Trichlorofluoromethane	75-69-4	●		
2,4,5-Trichlorophenol	95-95-4	●		
2,4,6-Trichlorophenol	88-06-2		●	
1,2,3-Trichloropropane	96-18-4	●		
Tridiphane	58138-08-2	●		
Trifluralin	1582-09-8	●		
Uranium, natural	7440-61-1		●	
Vanadium Pentoxide	1314-62-1	●		

Chemical	CASRN	RfD	CAR	HA
Vernam	1929-77-7	●		
Vinclozolin	50471-44-8	●		
Warfarin	81-81-2	●		
Xylenes	1330-20-7	●		
Zinc Cyanide	557-21-1	●		
Zinc Phosphide	1314-84-7	●		
Zineb	12122-67-7	●		

Appendix C

Sources of Information for Toxicity Profiles

TABLE C-1. TOXICITY PROFILES AVAILABLE FROM U.S. EPA OFFICE OF WASTE PROGRAMS ENFORCEMENT (OWPE) AND OFFICE OF EMERGENCY AND REMEDIAL RESPONSE (OERR)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
Acenaphthene	X	
Acenaphthylene	X	
Acetic acid	X	
Acetone	X	X
Acrolein	X	
Acrylonitrile	X	
Aldrin	X	
Anthracene	X	
Antimony	X	
Arsenic	X	X
Asbestos	X	X
Barium	X	X
Benzene	X	X
Benzidine	X	
Benzo(a)anthracene	X	
Benzo(a)pyrene		X
Benzothiazole	X	
Beryllium	X	
alpha-BHC	X	
beta-BHC	X	
gamma-BHC (lindane)	X	X
delta-BHC	X	
Butanol	X	
Butyl acetate	X	
Cadmium	X	X
Carbon tetrachloride	X	X
cis-Chlordane	X	X
trans-Chlordane	X	X
Chlorine	X	
Chlorobenzene	X	X
Chlorobenzilate	X	
Chloroethane	X	
Chloroform	X	X
p-Chloro-m-cresol	X	
1-Chloro-3-nitrobenzene	X	
bis(2-Chloroethoxy)ethane	X	
Chromium (total)	X	
Chromium (hexavalent)		X
Chromium (trivalent)		X
Chrysene	X	
Coal tars		X
Cobalt	X	
Copper	X	X
Cresol	X	X
Cyanides	X	X
Cyanuric acid	X	
p,p'-DDD	X	
o,p'-DDD	X	
p,p'-DDE	X	
p,p'-DDT	X	X
o,p'-DDT	X	X
Dibromochloropropane	X	
1,2-Dichlorobenzene	X	
1,3-Dichlorobenzene	X	
1,4-Dichlorobenzene	X	
1,1-Dichloroethane	X	X
1,2-Dichloroethane	X	X
1,1-Dichloroethylene	X	X
1,2-cis-Dichloroethylene		X
1,2-trans-Dichloroethylene	X	X
2,4-Dichlorophenol	X	
2,4-Dichlorophenoxyacetic acid	X	
1,2-Dichloropropane	X	

TABLE C-1. (Continued)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
1,3-Dichloropropane	X	
1,3-Dichloropropene	X	
Dicofol	X	
Dieldrin	X	
Diethyl benzene	X	
Diethylene glycol	X	
Diethyl phthalate	X	
Diisobutyl ketone	X	
Dimethylaminoethyl methacrylate	X	
Dimethyl aniline	X	
Dimethylnitrosamine	X	
2,4-Dimethyl pentane	X	
2,4-Dimethylphenol	X	
n-Dioctyl phthalate	X	
1,4-Dioxane	X	
Diphenyl ethane	X	
Endrin	X	
Ethanol	X	
bis(2-Chloroethyl) ether	X	
Ether	X	
Ethyl acetate	X	
Ethylbenzene	X	X
Ethylene glycol	X	
Ethyl hexanediol	X	
bis-2-Ethylhexyl phthalate	X	
Ethyl toluene	X	
Fluoranthene	X	
Formaldehyde	X	
Glycol ethers		X
Heptachlor	X	
Heptane	X	
Hexachlorobenzene	X	X
Hexachlorobutadiene	X	X
Hexachlorocyclohexane	X	
Hexachlorocyclopentadiene		X
Hexachloroethane	X	
Hexachlorophene	X	
Hexane	X	
Iron	X	X
Isobutyl alcohol	X	
Isopropyl benzene	X	
Isopropyl ether	X	
Lead	X	X
Lithium	X	
Magnesium	X	
Manganese	X	X
Mercury	X	X
Methacrylic acid	X	
Methanol	X	
Methyl chloride	X	
2-Methyl dodecane	X	
Methylene chloride	X	X
Methyl ethyl benzene	X	
Methyl ethyl ketone	X	X
3-Methyl hexane	X	
Methyl isobutyl ketone	X	
Methyl methacrylate	X	
Methyl parathion	X	
2-Methyl pentane	X	
3-Methyl pentane	X	
2-Methyl-1-pentene	X	
2-Methyl tetradecane	X	
2-Methyl tridecane	X	

TABLE C-1. (Continued)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
Monethanolamine	X	
Naphthalene	X	X
Nickel	X	X
Nitrocellulose	X	
2-Nitrophenol	X	
Pentachlorophenol	X	X
Pentadecane	X	
Phenanthrene	X	X
Phenol	X	X
Phenyl ether	X	
Phosphoric acid	X	
Phosphorus	X	
Picric acid	X	
Polychlorinated biphenyls (PCBs)	X	X
Polychlorinated dibenzo-p-dioxin	X	
Polycyclic aromatic hydrocarbons (PAHs)		X
Pyrene		X
Selenium	X	X
Silver	X	
Sodium chlorate	X	
Sodium cyanide		X
Sodium	X	
Stoddard solvent	X	
Sulfuric acid		X
1,2,4,5-Tetrachlorobenzene	X	
2,3,7,8-Tetrachloro-dibenzo-p-dioxin (TCDD)	X	X
1,1,2,2-Tetrachloroethane	X	X
Tetrachloroethylene	X	X
Tetraethyl lead	X	
Tetrahydrofuran	X	
Tetramethyl benzene	X	
Thallium	X	
Titanium	X	
Toluene	X	X
Toxaphene	X	
1,2,3-Trichlorobenzene	X	
1,2,4-Trichlorobenzene	X	
1,3,5-Trichlorobenzene	X	
2,3,6-Trichlorobenzoic acid	X	
1,1,1-Trichloroethane	X	X
1,1,2-Trichloroethane	X	X
Trichloroethylene	X	X
Trichlorofluoromethane	X	
2,4,5-Trichlorophenol	X	X
2,4,6-Trichlorophenol		X
2,4,5-Trichlorophenoxyacetic acid	X	
2,4,5-Trichlorophenoxy propionic acid	X	
Trimethylbenzene	X	
1,3,5-Trimethylbenzene	X	
1,2,4-Trimethylbenzene	X	
tris(2,3-Dibromopropyl)phosphate	X	
Undecane	X	
Vanadium	X	
Vinyl chloride	X	X
Xylene	X	X
m-Xylene	X	
o-Xylene	X	
p-Xylene	X	
Zinc	X	X

Reference: Life Systems (1985).

TABLE C-2. U.S. EPA SOURCES OF TOXICITY PROFILES

Document	Availability	Description
Criteria Document - Air	Office of Air Quality Planning and Standards (OAQPS)	Summary of the latest scientific knowledge on the effects of varying quantities of a substance in the air. Usually prepared for OAQPS by the Office of Health and Environmental Assessment (OHEA).
Criteria Document - Drinking Water	Office of Drinking Water (ODW)	Summary of important experimental results from the literature relevant to the chemistry and health effects of a specific drinking water contaminant. Serves as a foundation to support regulatory standards or guidelines for the acceptable concentration of the contaminant in the drinking water.
Criteria Document - Ambient Water Quality	Office of Water Regulations and Standards (OWRS)	Information on the type and extent of identifiable toxic effects on health and welfare expected from the presence of pollutants in any body of water. Objective of document is to protect most species in a balanced and healthy aquatic community and/or to protect human health.
Chemical Hazard Information Profile (CHIP)	Office of Toxic Substances (OTS)	Summary of readily available information concerning the health and environmental effects and potential exposure to a chemical.
Chemical Profile	Office of Waste Programs Enforcement (OWPE)	Brief summary of the chemical/physical properties, fate and transport, health effects and environmental toxicity levels for 202 chemicals identified at hazardous waste sites. Currently 183 of the planned Chemical Profiles are available in draft form.
Health Advisory	ODW	Develops toxicological analyses to establish an acceptable level in drinking water for unregulated contaminants for various exposure durations.
Health Assessment Document	Office of Health and Environmental Assessment (OHEA)	Inventories the scientific literature and evaluates key studies. Discusses dose-response relationships so that the nature of the adverse health response is evaluated in perspective with observed environmental levels. Usually prepared by OHEA for another office.
Health and Environmental Effects Profile	Office of Solid Waste (OSW)	Profiles are "mini-" criteria documents prepared usually as summaries of existing water quality criteria documents. They serve as a support for the listing of hazardous wastes in the RCRA program.
Health Effects Assessments	Office of Emergency and Remedial Response (OERR)	Summary of the pertinent health effects information on 58 chemicals found most often at hazardous waste sites. Developed by the Environmental Criteria and Assessment Office (ECAO) for OERR.

Address for all offices listed above: U.S. Environmental Protection Agency, 401 M Street S.W., Washington, DC 20460 (202) 382-2090

Reference: Life Systems (1985).

TABLE C-3. SELECTED CHEMICAL AND TOXICOLOGICAL DATABASES

Database vendor	Database Name	Database Contents	Access Procedures
MEDLARS (National Library of Medicine)	Toxline	1.5 million references on environmental and toxicological effects of chemicals.	Contact: MEDLARS Management Section National Library of Medicine 8600 Rockville Pike Bethesda, MD 20209 (301) 496-6193
	Chemline	An online chemical dictionary of 500,000 records.	
	RTECS (Registry of Toxic Effects of Chemical Substances)	Basic acute and chronic toxicity for more than 57,000 toxic chemicals.	
	AQUIRE (Aquatic Information Retrieval System	Toxicity data for 2,000 chemicals, each cross referenced by CAS number. Lists any studies on bioaccumulation, sublethal effects, and environmental fate of the chemical.	
CIS (Chemical Information System)	**CESARS (Chemical Evaluation Search and Retrieval System)**	Detailed toxicity and environmental fate information and evaluation on 150 chemicals of importance to Great Lakes.	Contact: CIS, Inc. Fein-Marquart Associates 7215 York Road Baltimore, MD 21212 (800) 247-8737
	CTCP (Clinical Toxicology of Commercial Products)	Ingredient and product information for most commercially available nonfood items.	
	Envirofate	Information on the environmental fate of approximately 500 chemicals.	
	ISHOR (Information System for Hazardous Organics in Water)	Physical and chemical properties of 14,000 organic compounds and associated aquatic toxicity data.	
	OHMTADS (Oil and Hazardous Materials Technical Assistance Data System)	Created by U.S. EPA Superfund. Includes information on environmental effects of 11,000+ hazardous substances.	

TABLE C-3. (Continued)

CAS Online (Chemical Abstracts)	Chemical Abstracts	Physical and chemical properties on 6 million chemical substances.	Contact: Chemical Abstracts Office Customer Service P.O. Box 3012 Columbus, OH 43210 (800) 848-6533
DOE/RECON	35 energy-related and environmental databases including Energy Database, Water Resources Abstracts, Environmental Mutagens, and Environmental Teratology.		Contact: Technical Information Center U.S. Department of Energy P.O. Box 62 Oak Ridge, TN 37380 (615) 575-1272

Reference: U.S. Fish and Wildlife Service (1986).

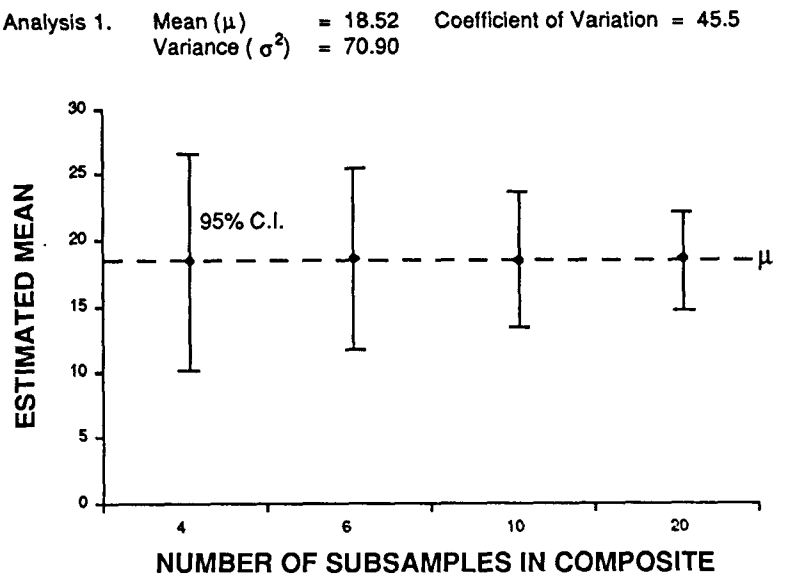
Appendix D

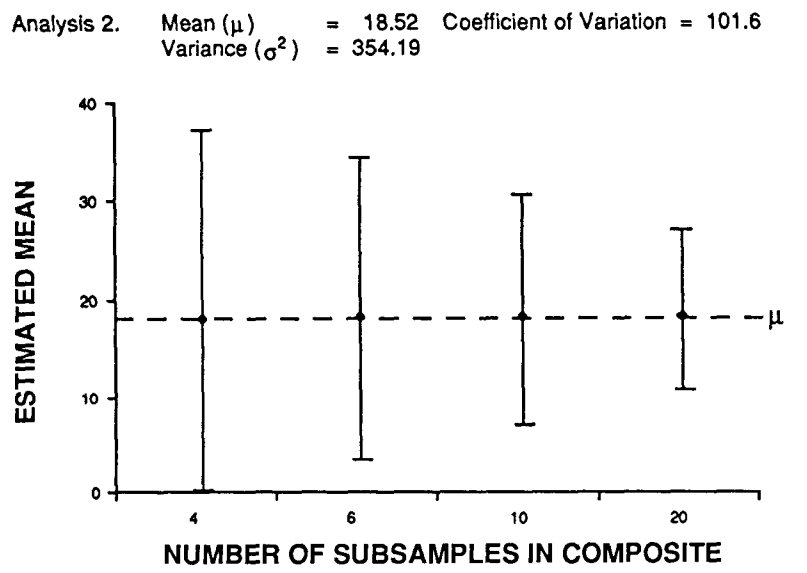
Evaluation of the Effects of Composite Sampling on Statistical Power of a Sampling Design

Tetra Tech (1986b) used simulation methods to make a direct comparison of grab and composite-sampling strategies. Simulation refers to the use of numerical techniques to generate random variables with specified statistical properties. For the analyses described below, Tetra Tech (1986b) developed computer programs to: 1) produce individual random samples from populations with normally distributed concentrations of contaminants, and other statistical properties similar to those of historical bioaccumulation data sets described in Tetra Tech (1986b), 2) construct composite samples, and 3) calculate statistical power of sampling designs using individual or composite samples.

Two sets of analyses were performed by Tetra Tech (1986b). In the first set, simulation methods were used to show the effect of sample compositing on the estimate of the population mean. Power analyses were used in the second set of analyses to demonstrate the effect of increasing the number of subsamples in a composite sample on the probability of detecting specified levels of differences among stations.

The first set of analyses demonstrated that the confidence in the estimate of the mean increases as the number of subsamples in the composite increases (Figure D-1). The simulated sampling consisted of randomly selecting 10,000 composite samples from two populations exhibiting two different levels of variability in the sampling environment. The mean value in both populations was fixed at 18.52, but the population variances were set at 70.90 or 354.19, corresponding to coefficients of variation of 45.5 and 101.6, respectively. These popula-





Reference: Tetra Tech (1986b)

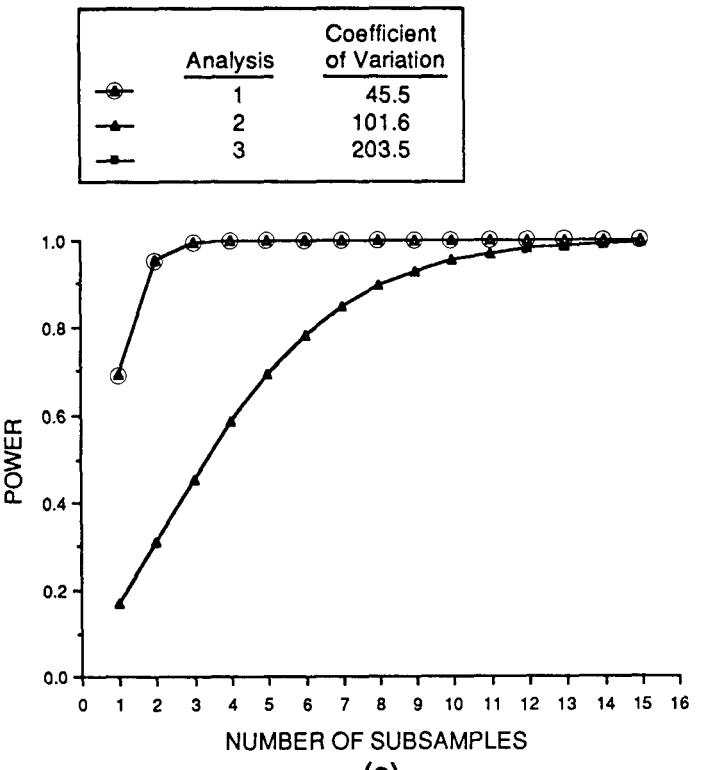
Figure D-1 Effects of increasing composite sample size on confidence in the estimate of the mean.

tion characteristics were selected as representative of the range of values for the coefficient of variation observed in the historical data sets for selected metals and organic compounds in marine organisms (Tetra Tech 1986b). For a series of individual fish samples taken from the corresponding populations used in Analysis 1, the 95 percent confidence intervals would range from 1.7 to 35.4 concentration units (e.g., ppm).

To demonstrate the effect of sample compositing on the power of the statistical test of significance, Tetra Tech (1986b) performed statistical power analyses using a one-way Analysis of Variance (ANOVA) model. In these analyses (Figure D-2), the number of stations (5), number of replicate composite samples at each station (5), significance level of the test (0.05), residual error variance level, and level of minimum detectable difference (100 percent of overall mean) were fixed. The power of the test (i.e., the probability of detecting the specified minimum difference) was then calculated as a function of the number of subsamples constituting each replicate composite sample.

Power analyses were conducted for three levels of sample variability. All design parameters except the residual error variance were identical in each set of analyses. Values of the residual error variance were selected to represent the range of values found in the historical data sets described by Tetra Tech (1986b). The coefficients of variation selected for these three sets of analyses were 45.5, 101.6, and 203.5.

As shown in Figure D-2, the probability of statistically detecting a difference equal to the overall sample mean among stations increases with the collection of replicate composite samples at each station and as the number of subsamples constituting the composite increases. The results of both sets of analyses shown in Figure D-2 also demonstrate the phenomenon of diminishing returns for continued increases in the number of subsamples per composite. In Analysis Set 1, for example, virtually no increase in the power of the statistical test was achieved with increasing the subsample size above three. In the second analysis set, substantial increases in statistical power were achieved by increasing the number of subsamples in each composite from 2 to 10. However, with each successive increase in subsample size, the relative benefit was reduced until very little was gained by increasing the subsample size above 10. For moderate levels of variability, 6-10 subsamples within each of 5 replicate composite samples may be adequate to detect a treatment difference equal to 100 percent of the mean among treatments. At the highest level of variability analyzed, the collection of replicate composite samples composed of 25 subsamples each is required to obtain a testing power of 0.80 (Figure D-2).



Reference: Tetra Tech (1986b)

Figure D-2 Power of statistical tests vs. number of subsamples in composite replicate samples. Fixed design parameters: number of stations = 5, number of replicates = 5, significance level = 0.05, minimum detectable difference = 100 percent of overall mean value.

Appendix E

Evaluation of the Effects of Sample Replication on Statistical Power of a Sampling Design

Statistical power analysis can be used to evaluate alternative sampling designs with varying levels of replication (Cohen 1977; Gordon et al. 1980; Tetra Tech 1986b). In statistical power analysis, relationships among the following study design parameters are evaluated:

- **Power** - Probability of detecting a real difference among treatments (e.g., species, stations, times)
- **Type I error** (α) - Probability of wrongly concluding that there are differences among treatments
- **Minimum detectable difference** - Magnitude of the smallest difference that can be detected for given power and Type I error
- **Residual error** - Natural variability
- **Number of stations**
- **Number of replicate samples.**

The analyses presented below were conducted with the objective of providing guidance in selecting levels of sampling replication. This objective was addressed by determining the magnitudes of difference among variables that can be reliably detected with varying levels of sampling effort. A one-way ANOVA model was used to evaluate statistical sensitivity relative to level of sample replication. Tetra Tech (1986b,d) provides details of the ANOVA model and results of the analyses. All power analyses were conducted using the Ocean Data

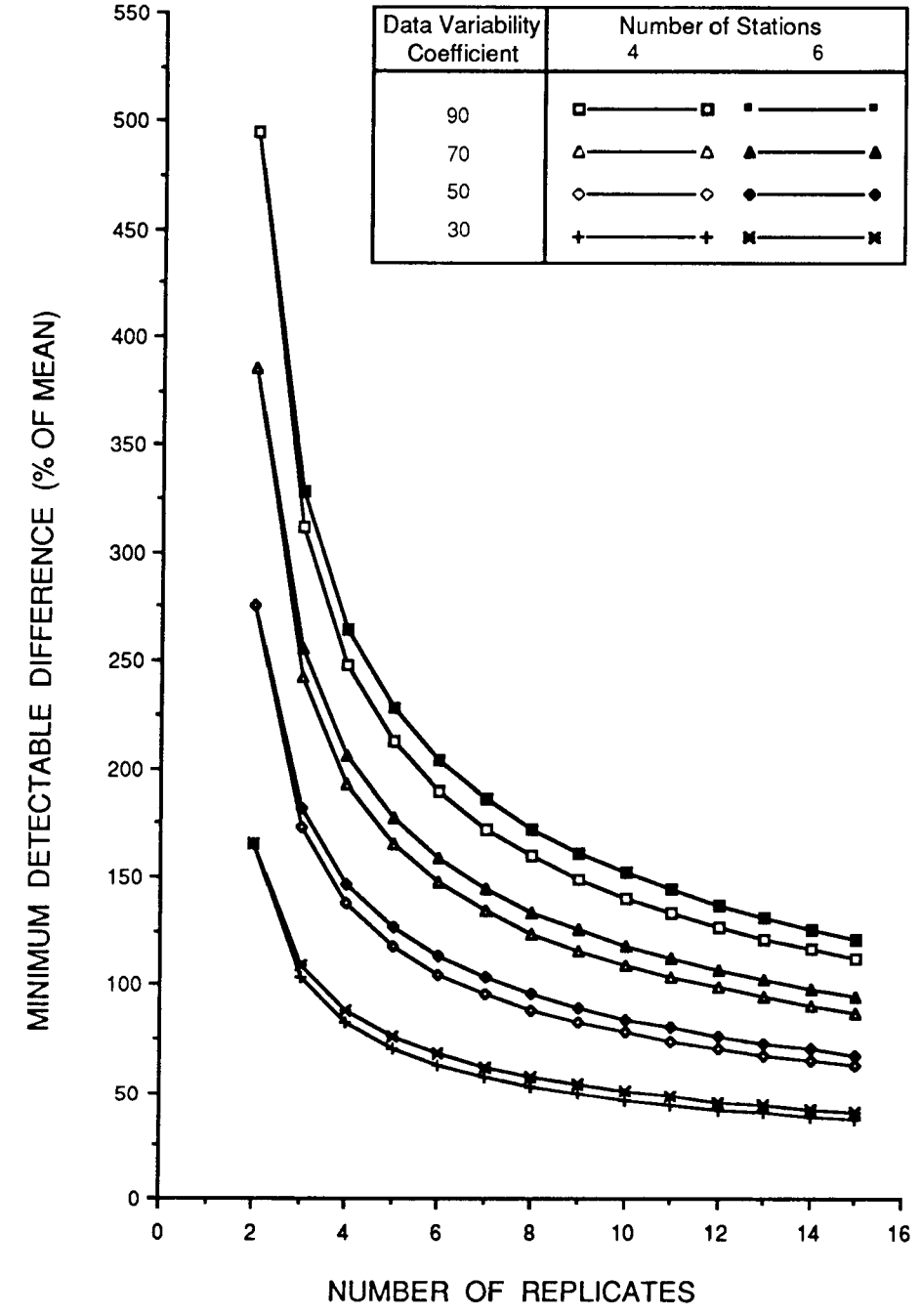
Evaluation System (ODES) maintained by EPA's Office of Marine and Estuarine Protection (Tetra Tech 1986d). The measure used to evaluate the statistical sensitivity of the monitoring design was the minimum detectable difference between two mean values. To generalize the results of the power analysis, the minimum detectable difference was expressed as a percentage of the grand mean among treatments. The power of the test was fixed at 0.80.

Predicted values of minimum detectable difference are shown for various levels of sample replication in Figures E-1 and E-2. For these analyses, the Type I error was fixed at 0.05. Minimum detectable difference was plotted vs. number of replicate samples for the following cases:

- Number of stations (or sampling times) equal to 4, 6, 8, and 16 stations (or times)
- Data Variability Coefficient (across treatments) equal to 30, 50, 70, and 90 percent.

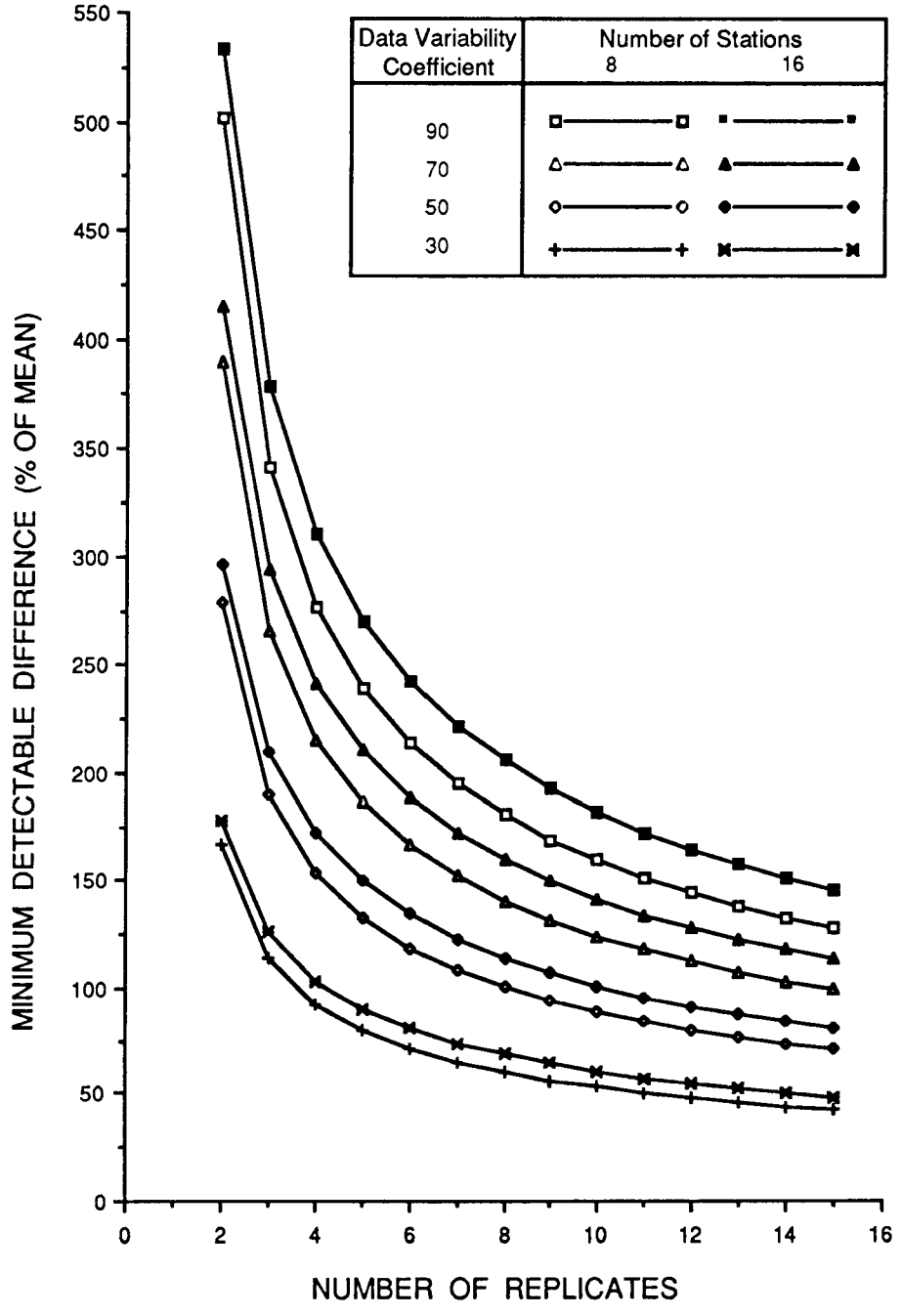
The Data Variability Coefficient is equal to the within-groups mean square divided by the grand mean among groups (and multiplied by 100 to convert to a percentage). In designing a bioaccumulation study, the Data Variability Coefficient can be estimated by performing an ANOVA on available data from the literature or on a preliminary data set. If such data cannot be obtained, the average Coefficient of Variation (within groups) can be used as a rough estimate of the Data Variability Coefficient.

The effect of setting a different value for Type I error is shown in Figure E-3. The effect of changes in Type I error is greater for higher levels of data variability. Note that substantial increases in sensitivity (i.e., decreases in minimum detectable difference) are achieved only for the case of three replicate samples in Figure E-3.



Reference: Tetra Tech (1986b)

Figure E-1 Minimum detectable difference versus number of replicates at selected levels of unexplained variance for 4 and 6 stations. Power of test = 0.80, significance level = 0.05.



Reference: Tetra Tech (1986b)

Figure E-2 Minimum detectable difference versus number of replicates at selected levels of unexplained variance for 8 and 16 stations. Power of test = 0.80, significance level = 0.05.

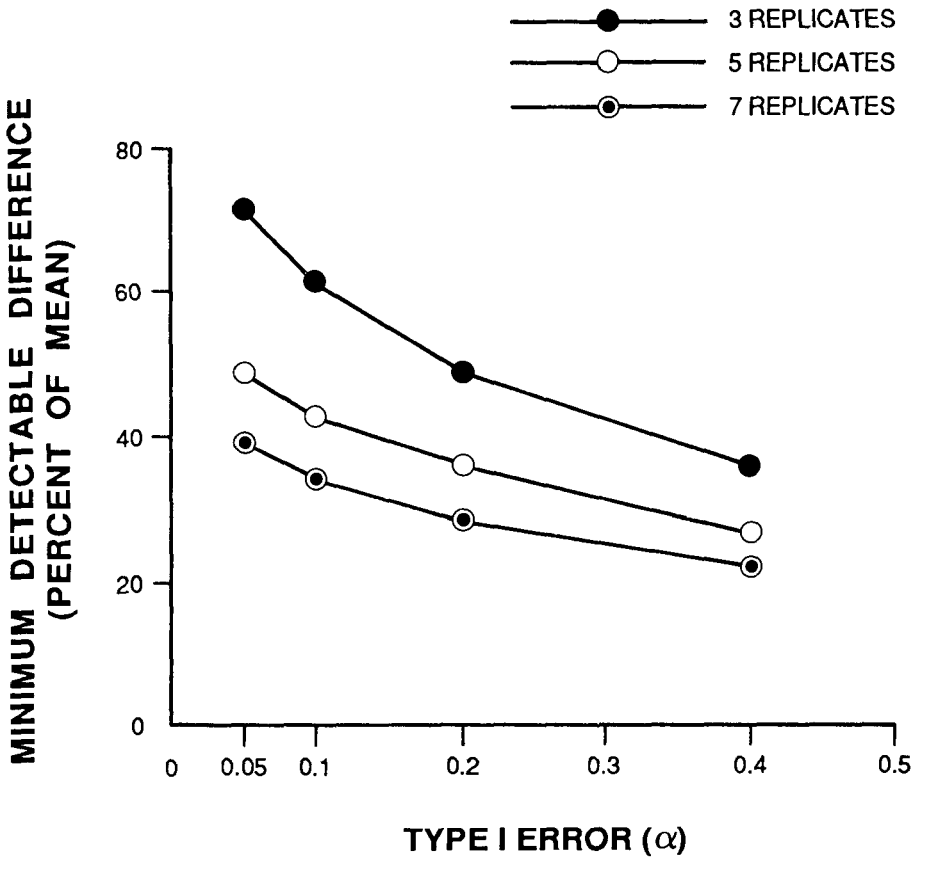


Figure E-3 Minimum detectable difference versus Type I Error for one-way ANOVA design with 3, 5, and 7 replicate samples.

Appendix F

Estimation of Fish/Shellfish Consumption from a National Database

The EPA Office of Pesticide Programs (OPP) has evaluated comprehensive data on dietary consumption of fish and shellfish within the conterminous United States. Selected consumption rate data for the U.S. population were used to provide an overview of potential exposure of humans to toxic chemicals associated with the consumption of contaminated fish and shellfish. Many surveys and reports were examined to determine probable sources for data on patterns of fish and shellfish consumption. Some economic reports are useful only for estimating average fish and seafood consumption. In contrast, polls have the potential to provide estimates of individual consumption trends by consumer, ethnic, or geographical subgroup (Table 1).

Development of a National Database

Based on sample size and relevance to recent trends in fish consumption, OPP concluded that the most reliable database for average daily consumption of fish and shellfish was the U.S. Department of Agriculture (USDA) Nationwide Food Consumption Survey of 1977-1978. In addition to being relatively recent, the USDA survey had a weighted sample size of 36,000 individuals. The consumption values listed in this survey are based on 3 days of individual consumption (from a 1-day recall and a 2-day diary) gathered by interviewers over the course of 1 year. Although the USDA 1977-1978 National Food Consumption Survey is an excellent source of fish consumption data, this survey was conducted 9-10 years ago. Fish consumption in the United States has been rising slowly for several years. Based upon the USDA 1977-1978 survey and their National Food Consumption Survey CSFII Report No. 85-3, the U.S. National Marine Fisheries Services estimated that

average per capita consumption of fish and shellfish increased from 13 g/day in 1960 to 21 g/day in 1986. Because of the nature of these surveys and limitations of polls in terms of duration of individual records and numbers of people surveyed, precise statistical distributions for lifetime fish consumption cannot be obtained with existing data.

Consumption values derived from the 1977-1978 USDA study were used to develop EPA's Tolerance Assessment System (TAS). Mean and percentiles of fish and shellfish consumption rates are provided in TAS for the U.S. population in the 48 conterminous states and various population subgroups (Tables 2-7). These estimates are for "acute" consumption (i.e., the amount of fish eaten in a single day). The average per capita fish/shellfish consumption rate of 15 g/day in TAS (No. 4 of Table 1) is generally consistent with the per capita consumption values listed for other surveys and reports.

The distribution of consumption provided in Tables 2-7 is the distribution among fish or shellfish eaters only, and is not a distribution for the entire population. The column titled "% Population as Consumers" provides the percentage of each population subgroup that is estimated to be a consumer of each category of fish/shellfish on any given day. The mean consumption estimates shown in Tables 2-7 are also for eaters only, and should not be confused with the mean per capita consumption estimates that are more commonly used in TAS analyses. These numbers provide valid estimates of the amounts of fish eaten in a single day. However, because of the way the data were derived, the frequency of fish consumption and, hence, annual consumption applies only to the "average" person. It is not possible to predict from that survey the population distribution for frequency of consumption and range in annual consumption.

Estimation of Local Consumption

Since the estimates of fish consumption just discussed are national averages, they are not predictive of all subgroups and regions on a scale fine enough to address local situations of potential concern. If local fish consumption information is not available, the Fish Contamination Subcommittee of the Risk Assessment Council suggests that other estimates of extreme consumption can be made by assuming that fish consumption by some subgroups would be equal to the average consumption of red meat (130 g/day) and, as a "reasonable" worst case, that some people would consume fish at levels equal to the combined TAS average consumption of red meat, poultry, and fish/shellfish (180 g/day) (Table 8). Conceivably, these values could be exceeded locally, especially when economically disadvantaged people rely on fishing to survive. Adding on an additional equivalent for egg consumption would bring the average estimate up to 215 g/day, and this might not be unreasonable for special situations. The above values are based on consumption by an average 60-kg individual.

Based on 114 g (0.25 pound) for a single serving of fish/shellfish, an average annual consumption of 18 g/day (e.g., see Data Source Nos. 12 and 13 of Table 1) corresponds to approximately 1 meal per week of fish or shellfish. Using the TAS estimate of 180 g/day for total meat protein consumption (consisting of red meat, poultry, and

fish/shellfish), and an estimate of 114 g for an average single serving, the total average meat consumption corresponds to about 11 meals per week.

References

Dykstra, William. January 12, 1982. "Ferriamicide; Request for Conditional Registration; EPA Reg. No. 38962-RR", Internal Memorandum to George LaRocca.

Environ Corporation. 1985. "Fish Consumption by Recreational Fishermen: An Example of Lake Ontario/Niagara River Region." Prepared for USEPA Office of Enforcement and Compliance Monitoring.

Finch, R., 1973. "Effects of Regulatory Guidelines on the Intake of Mercury from Fish" - the MECCA Project, NMFS, Fishery Bulletin, Vol. 71, No. 3, pp. 615-626.

Metzger, Michael., March 25, 1987. "Fish Action Level Reevalution for Aldrin/Dieldrin, Chlordane, DDT, Heptachlor, and Mirex." No Accession Number RCB Numbers 2058, 2062, 2063, 2064, 2065 and 2066.", Internal Memorandum to Jack Housenger.

Ontario Ministry of the Environment. 1984. Guide to Eating Ontario Sport Fish, 1984-1985. Southern Ontario, Great Lakes.

Page, N.; Cavender, F.; Cook, B. 1985. "Carcinogenic Rish Assessment for Aldrin and Dieldrin." Unpublished study prepared by Dynamac Corp. under EPA Contract No. 68-02-4131.

Sonstegard, R., Tufts University, Boston, Massachusetts. Personal communication.

SRI International. 1980. "Seafood Consumption Data Analysis (Final Report)." Prepared for USEPA, under EPA Contract No. 68-01-3887.

USDA. 1984. "Consumption and Family Living," Agricultural statistics., Table 697, p. 506.

USDA. 1985. "Food Consumption, Prices and Expenditures." ERS, Statistical Bulletin 749. Table 7, p. 13.

USDA. 1985. Nutrition Monitoring Division, Human Nutrition Information Service. Food and Nutrient Intakes: Individuals in Four Regions, 1977-1978. Report No. I-3.

USDA. 1986. Nationwide Food Consumption Survey Continuing Survey of Food Intakes by Individuals, Men 19-50 Years, 1 Day 1985. NFCS, CSFII Report No. 85-3.

USDA. 1986. Nationwide Food Consumption Survey Continuing Survey of Food Intakes by Individuals, Low-Income Women 19-50 Years and Their Children 1-5 Years, 1 Day 1985. NFCS, CSFII Report No. 85-2.

USDA. 1987. Nationwide Food Consumption Survey Continuing Survey of Food Intakes by Individuals, Women 19-50 Years and Their Children 1-5 Years, 1 Day 1986. NFCS, CSFII Report No. 86-1.

USDC. 1987. National Oceanic and Atmospheric Administration, National Marine Fisheries Service. Fisheries of the United States, 1986, Current Fisheries Statistics No. 8385.

Table 1: Fish Consumption Data Summary
Survey Data

Source	Survey Date[1]	Average Consumption g/day	Extreme Consumption g/day	Caveats
1. USDA Nationwide Food Consumption Survey (for individuals) note: Figure obtained from Environ 1985	1977-1978	12.0		Sample size >36,000 (weighted). Fish and shellfish in the conterminous 48 states. Based on a three day survey that included a 1 day recall and a 2 day diary.
2. USDA Nationwide Food Consumption Survey Continuing Survey of Food Intakes by Individuals Report #85-3	1985	21 14 (from 1977-1978 survey above)		Sample size = 658 for men 19-50 only. 1 day recall. Fish and shellfish.
3. USDA NFCS, CSFII Report #86-1	1986	11 13 (from a CSFII conducted in 1985) 11 (from 1977-1978 survey above)		Sample size = 1501 women and 509 children. This survey included women 19-50 and their children 1-5. 1 day recall. Fish and shellfish.
4. USDA NFCS, CSFII Report #85-2	1985	11 (women) 5 (children)		Sample size = 2,210 women, 1,314 children. This survey included low income women 19-50 and their children 1-5. Fish and shellfish. 1 day recall.
5. EPA Tolerance Assessment System (computed for a 60kg individual) a. Total b. Freshwater finfish note: Although the USDA survey figure listed is for fish and shellfish, the TAS data summary includes roe and caviar as well. It is unclear whether the USDA figure of 12 g/day obtained from Environ 1985 includes ore and caviar.	1977-1978		15.2 1.8	Based on USDA 19077-1978 NFCS survey. The discrepancy between TAS's 15.2 g/day and the USDA's 12 g/day is due to conversion of the TAS figure from g/kg body weight/day to g day by multiplying by 60 kg.

[1] Those dates which reflect publication or communication rather than the date of the survey are enclosed in parenthesis

Table 1 (cont.): Fish Consumption Data Summary
Survey Data

Source	Survey Date	Average Consumption g/day	Extreme Consumption g/day	Caveats
6. USDA's Foods Commonly Eaten by Individuals: Amounts Per Day and Per Eating Session	(1982)	54		Consumers of finfish other than canned, dried or raw. Mean does not equal the median. Sample size?
a. 50th percentile			38	
b. 90th percentile			96	
c. 95th percentile			132	
d. 99th percentile			221	
note: Obtained from Environ 1985				
7. National Purchase Diary (analyzed by SRI International)	1973-1974			Sample size = greater than 25,000. 1/12 of the sample was surveyed each month. It appears that this survey was for the conterminous 48 states. The SRI analysis and figures were only for fish consumers.
a. 95th percentile			41.7	
note: Obtained from SRI International. It is unclear whether the sample size of 25,000 included nonconsumers as well as consumers of fish.		14.3		
8. National Marine Fisheries Service Market Facts Survey	1969-1970			Sample size = 4,864. Survey yielded a per capita fish consumption figure. It is not clear whether recreationally caught fish are included. Representative household completed diaries twice a month for 1 year regarding fish consumption patterns at home and outside the home.
a. 99th percentile			77	
b. 99.9th percentile		16.8	165	
note: The average value of 16.8 g/day was derived from Environ, and the extreme figures came form Roland Finch's article listed in the reference section. There is a discrepancy between the 16.8 figure and the average figure of 14 g/day based on the same survey cited by Finch.				
9. Guide to Eating Ontario Sport Fish	1983			Sample size unknown. Self selection biases possible. This survey is for Ontario fishermen consumption of freshwater finfish.
		13.8		

Table 1 (cont.): Fish Consumption Data Summary
Survey Data

Source	Survey Date	Average Consumption g/day	Extreme Consumption g/day	Caveats
10. Environ 1985 Estimate of Humphrey's Lake Michigan Data	(1976)	45		Estimate is extremely rough, and is for Lake Michigan sports fishermen consumption of Lake Michigan fish. Subjects were selected because of how much fish they caught.
11. Personal Communication with R. Sonstegard concerning intensive Lake Ontario sports fishermen.	1987		373	Intensive Lake Ontario sports fishermen.
		TAS MEAT CONSUMPTION VALUES (g/day)		
		a. Red meat	134	
		b. Poultry	30.4	
		c. Fish	15.2	
12. USDA Agricultural Statistics note: Unclear what fish connotes.	1983	18.4		Per capita market data. Retail weight. Fish.
13. USDA ERS, Statistical "Food Consumption, Prices, and Expenditures." note: Unclear whether seafood other than fish and shellfish included.	1985	18.0		Per capita market data. Edible weight. Fish and shellfish.
14. National Marine Fisheries Service Current Fisheries Report	1986 1985 1984 1960	18.3 17.9 17.0 10.3		Commercial fish and shellfish per capita. The military population is excluded and no information on fish caught through noncommercial activities.
a. Recreationally caught fish consumption cited in 1986 Current Fisheries Report table footnote and not included in that table	1970	3.7-5.3		
15. New York State Department of Environmental Conservation Average Fish Consumption for Recreational Fishermen. note: From Environ 1985.	?	32.4		Based on 90th percentile of nationwide fish consumption figures. The source of the figures is not known. Survey

Table 2: Consumption of Freshwater Finfish

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X=															
			0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	1.10	2.7038	100	100	98	97	93	87	79	72	64	58	51	30	17	10	2	0	0
INFANTS(<1 YEAR)	0.11	2.6724	100	100	100	100	100	100	100	100	100	44	44	44	44	0	0	0	0
CHILDREN(1-6 YRS)	0.62	4.8498	100	100	100	99	98	96	93	93	92	89	84	68	50	32	8	3	0
FEMALES(13+ YRS)	1.14	2.4986	100	100	98	97	93	87	78	69	62	55	48	27	14	7	2	0	0
MALES(13+ YRS)	1.37	2.5524	100	100	98	95	91	84	77	70	61	54	47	27	15	8	1	0	0

Table 3: Consumption of Saltwater Finfish

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X=															
			0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	10.73	1.7510	100	97	91	84	75	65	56	47	40	35	30	14	7	4	0	0	0
INFANTS(<1 YEAR)	0.93	4.5676	100	100	95	89	83	77	77	66	65	58	58	58	51	45	6	0	0
CHILDREN(1-6 YRS)	9.36	3.4117	100	99	96	93	90	86	82	78	74	71	67	46	30	20	3	1	0
FEMALES(13+ YRS)	11.69	1.4970	100	97	90	82	72	61	51	41	34	28	23	9	4	1	0	0	0
MALES(13+ YRS)	10.32	1.5181	100	97	90	81	71	61	51	41	34	29	25	10	4	2	0	0	0

Table 4: Consumption of Saltwater Finfish - Dried

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.02	0.4758	100	26	26	26	26	26	26	26	6	0	0	0	0	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.02	0.4511	100	25	25	25	25	25	25	25	13	0	0	0	0	0	0	0	0
MALES(13+ YRS)	0.03	0.5016	100	27	27	27	27	27	27	27	0	0	0	0	0	0	0	0	0

Table 5: Consumption of Fish-Roe, Caviar

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.01	2.3449	100	100	100	100	85	85	85	69	69	69	69	38	15	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.01	2.5632	100	100	100	100	100	100	100	100	100	100	100	42	0	0	0	0	0
MALES(13+ YRS)	0.00	0.7346	100	100	100	100	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 6: Consumption of Shellfish

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	2.61	1.3313	100	88	76	64	55	47	41	34	28	24	21	9	4	2	0	0	0
INFANTS(<1 YEAR)	0.11	0.8432	100	100	100	49	49	49	49	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.98	2.1878	100	90	80	71	64	61	59	55	52	49	43	22	13	11	1	0	0
FEMALES(13+ YRS)	2.98	1.3156	100	87	75	64	56	46	39	34	28	24	21	9	4	2	0	0	0
MALES(13+ YRS)	3.10	1.2159	100	88	76	64	53	44	39	30	25	21	17	7	4	2	0	0	0

Table 7: Consumption of Fish-Unspecified

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.02	1.6519	100	100	96	96	69	60	60	56	46	40	28	12	5	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.02	1.9775	100	100	100	100	79	79	79	79	79	64	43	18	0	0	0	0	0
MALES(13+ YRS)	0.03	0.9956	100	100	92	92	54	35	35	26	7	7	0	0	0	0	0	0	0

Table 8: Fish Consumption - TAS

		g/day/kg body weight	g/day[1]	meals/year[1]	(assuming a meal size of approximately 4 ounces or 114 grams)
1.	EPA TAS Average Per capita Fish/shellfish	0.25	15	48	
2.	EPA TAS Average Per capita Red meat	2.2	130	420	
3.	EPA TAS Average Per capita Red Meat + Poultry + Fish	3.0	180	580	

[1] Based on TAS values for average consumption presented in g/day/kg body weight and adjusted to g/day for a 60 kg individual.

Appendix G

EPA Office of Research and Development

ENVIRONMENTAL RESEARCH LABORATORIES

Region 1

Environmental Research Laboratory/ORD
South Ferry Road
Narragansett, RI 02882
FTS: 8-838-5087
DDD: (401) 789-1071

Region 4

Environmental Research Laboratory/ORD
Sabine Island
Gulf Breeze, FL 32561
FTS: 8-686-9011
DDD: (904) 932-5311

Environmental Research Laboratory/ORD
College Station Road
Athens, GA 30613
FTS: 8-250-3134
DDD: (404) 546-3134

Region 5

Environmental Research Laboratory/ORD
6201 Congdon Boulevard
Duluth, MN 55804
FTS: 8-780-5550
DDD: (218) 720-5550

Environmental Ecological and Support Laboratory/ORD
26 W. St. Clair Street
Cincinnati, OH 45268
FTS: 8-684-7301
DDD: (513) 569-7301

Center for Environmental Research Information/ORD
26 West St. Clair Street
Cincinnati, OH 45268
FTS: 8-684-7391
DDD: (513) 569-7391

Region 6

Robert S. Kerr Environmental Research Laboratory/ORD
P.O. Box 1198
Ada, OK 74820
FTS: 8-743-2011
DDD: (405) 332-8800

Region 10

Environmental Research Laboratory-Corvallis/ORD
200 S.W. 35th Street
Corvallis, OR 97333
FTS: 8-420-4601
DDD: (503) 757-4601

Pacific Division - Environmental Research Lab/ORD
Hatfield Marine Science Center
Marine Science Drive
FTS: 8-867-4040
DDD: (503) 867-4040

Appendix H

Compilation of Legal Limits for Chemical Contaminants in Fish and Fishery Products

TABLE H-1. COMPILATION OF LEGAL LIMITS FOR HAZARDOUS METALS IN FISH AND FISHERY PRODUCTS

	Metals (ppm)								
Country	As	Cd	Cr	Cu	Hg	Pb	Sb	Se	Zn
Australia	1.0,1.5[b]	0.2-5.5		10-70	0.5,1.0	1.5-5.5	1.5	1.0,2.0	40-1,000
Brazil					0.5[c]				
Canada	3.5				0.5	0.5			
Chile	0.12,1.0	0.5		10		2.0		0.05,0.3	100
Denmark					0.5				
Ecuador	1.0			10	1.0	5.0			
Finland	5.0				1.0	2.0			
France					0.5,0.7				
Germany		0.5			1.0	0.5			
Greece					0.7				
Hong Kong	1.4-10	2.0	1.0		0.5	6.0	1.0		
India	1.0			10	0.5[c]	5.0			50
Israel					0.5				
Italy					0.7[c]	2.0			
Japan					0.3,0.4[c]				
Korea					0.5				
Netherlands		0.5-1.0			1.0[c]	0.5,2.0			
New Zealand	1.0	1.0		30	0.5[c]	2.0	1.0	2.0	40
Philippines	30				0.5	0.5			
Poland	4.0			10-30		1.0-2.0			30-50
Spain					0.5				
Sweden					1.0[c]	1.0-2.0			
Switzerland		0.1			0.5	1.0			
Thailand	2.0			20	0.5	1.0			
United Kingdom	1.0			20		2.0-10			50
United States					1.0[c]				
U.S.S.R.					0.2-1.0				
Venezuela	0.1	0,0.1		10	0.1-0.5	2.0			
Zambia	3.5-5.0			100	0.2-0.3	0.5-10			100
Range									
Minimum	0.1	0	1.0	10	0.1	0.5	1.0	0.05	30
Maximum	10	5.5	1.0	100	1.0	10	1.5	2.0	1,000

[a] Limit varies among states.
[b] Inorganic.
[c] Total.

References: Nauen (1983); U.S. Food and Drug Administration (1982, 1984).

TABLE H-2. COMPILATION OF LEGAL LIMITS FOR ORGANIC PRIORITY POLLUTANTS AND PESTICIDES IN FISH AND FISHERY PRODUCTS (ppm)

	Hexa-chloro-benzene	PCBs	TCDD	Aldrin/ Dieldrin	Chlor-dane	DDT	DDE	DDD	DDIs	Endrin	Heptachlor/ Heptahclor-epoxide	Kepone	HCH (Lindane	Mala-thian	Mirex	Parathion	Toxaphene	Vinyl Cloride
Canada		2.0	20[a]	0.1[b]	0.1[b]	5.0	5.0	5.0	5.0	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	
Denmark						2.0-5.0												
Germany[c]	0.5			0.5-1.0	0.01				2.0-5.0	0.01	0.01		2.0		0.01			
Iceland													0.5					
Netherlands		5.0																
Sweden	0.2	2.0-5.0		0.1					5.0				0.2					0.01
Switzerland		1.0																
Thailand				0.1,0.3		5.0				0.3	0.3		0.5	0.6		0.2		
United States		2.0		0.3	0.3	5.0	5.0	5.0	5.0	0.3	0.3	0.3-0.4			0 .1		5.0	
Range																		
Minimum	0.2	1.0	20[a]	0.1	0.01	2.0	5.0	5.0	2.0	0.01	0.01	0.1	0.1	01.	0.1	0.1	0.1	0.01
Maximum	0.5	5.0	20[a]	1.0	0.3	5.0	5.0	5.0	5.0	0.3	0.3	0.4	2.0	0.6	0.1	0.2	5.0	0.01

[a] ppt (parts per trillion).
[b] Legal limit exists for agricultural chemicals in general.
[c] Legal limits exsit for other organic chemicals that are not priority pollutants (see references).

Reference: Nauen (1983); U.S. Food and Drug Administartion (1982, 1984).